

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: JANIA HINES Examiner #: _____ Date: 9/4/90
 Art Unit: 645 Phone Number 305-0481 Serial Number: 091,141
 Mail Box and Bldg/Room Location: DMH 14217 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Assay for Carbohydrate-Free transferrin

Inventors (please provide full names): EELING SUNDRE HAGEN

Earliest Priority Filing Date: 10/6/1997

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

siderophilin alcoholism alcohol-drinking consumption
transferrin D12.776.124.50,800 D12.776.157.890 D12.776.556.901
D12.776.377.715.182.831 D12.776.124.790.323.835

carbohydrate free transferrin (CDT)

asialo, monosialo, trisialo, tetrasialo, pentasialo
disialo transferrin

carbohydrate deficient transferrin

Point of Contact:

Mary Hale

Technical Info. Specialist

CM1 12D16 Tel: 308-4258

alcohol^(a) drinking C21.739.100,250
F1.145.317.269 F3.900.100.350

alcoholism drug dependence
temperance?

alcohol consumption

1041
1024-34
44

Please search the claims and inventor.

Thanks.

STAFF USE ONLY

Searcher: Mary

Searcher Phone #: _____

Searcher Location: _____

Date Searcher Picked Up: _____

Date Completed: 9/1/93

Searcher Prep & Review Time: 6

Clerical Prep Time: _____

Online Time: 25

Type of Search

Vendors and cost where applicable

NA Sequence (#) _____ STN 308-56

AA Sequence (#) _____ Dialog _____

Structure (#) _____ Questel/Orbit _____

Bibliographic ✓ Dr. Link _____

Litigation _____ Lexis/Nexis _____

Fulltext _____ Sequence Systems _____

Patent Family _____ WWW/Internet _____

Other _____ Other (specify) _____

Best Available Copy

J. HINES
464158

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.15	0.15

FILE 'REGISTRY' ENTERED AT 10:24:17 ON 13 SEP 2000
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2000 American Chemical Society (ACS)

STRUCTURE FILE UPDATES: 12 SEP 2000 HIGHEST RN 288839-14-5
DICTIONARY FILE UPDATES: 12 SEP 2000 HIGHEST RN 288839-14-5

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 11, 2000

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT
for details.

=> e transferrin/cn 5

E1	1	TRANSFERCAT/CN
E2	1	TRANSFERIN KW/CN
E3	0 -->	TRANSFERRIN/CN
E4	1	TRANSFERRIN (206-GLUTAMINE) (HUMAN) /CN
E5	1	TRANSFERRIN (207-GLUTAMIC ACID) (HUMAN) /CN

=> e carbohydrate free transferrin/cn 5

E1	1	CARBOHYDRASE/CN
E2	1	CARBOHYDRATASE/CN
E3	0 -->	CARBOHYDRATE FREE TRANSFERRIN/CN
E4	1	CARBOHYDRATE ISOMERASE, KPSF/GUTQ FAMILY (CHLAMYDIA
MURIDARU		M STRAIN NIGG GENE TC0679) /CN
E5	1	CARBOHYDRATE ISOMERASE, KPSF/GUTQ FAMILY (CHLAMYDOPHILA
PNEU		MONIAE AR39 STRAIN AR39 GENE CP0226) /CN

=> s ?transferrin?/cns

L1 443 ?TRANSFERRIN?/CNS

=> fil medl,capplus,biosis,embase,wpids,jicst

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	4.20	4.35

FILE 'MEDLINE' ENTERED AT 10:25:24 ON 13 SEP 2000

FILE 'CAPPLUS' ENTERED AT 10:25:24 ON 13 SEP 2000
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
Prepared by M. Hale 308-4258

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2000 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOSIS' ENTERED AT 10:25:24 ON 13 SEP 2000
COPYRIGHT (C) 2000 BIOSIS(R)

FILE 'EMBASE' ENTERED AT 10:25:24 ON 13 SEP 2000
COPYRIGHT (C) 2000 Elsevier Science B.V. All rights reserved.

FILE 'WPIDS' ENTERED AT 10:25:24 ON 13 SEP 2000
COPYRIGHT (C) 2000 DERWENT INFORMATION LTD

FILE 'JICST-EPLUS' ENTERED AT 10:25:24 ON 13 SEP 2000
COPYRIGHT (C) 2000 Japan Science and Technology Corporation (JST)

=> s (l1 or ?transferrin? or siderophilin? or (d12.775.124.50.800 or d12.776.157.890 or d12.776.377.715.192.839 or d12.776.556.901/ct) and (alcoholism or alcohol(2a)(consump? or drink?) or temperance or drug dependence or (f1.145.317.269 or c21.739.100.250 or f3.900.100.350)/ct)

UNMATCHED LEFT PARENTHESIS '(L1'

The number of right parentheses in a query must be equal to the number of left parentheses.

=> s (l1 or ?transferrin? or siderophilin? or (d12.775.124.50.800 or d12.776.157.890 or d12.776.377.715.192.839 or d12.776.556.901/ct)) and (alcoholism or alcohol(2a)(consump? or drink?) or temperance or drug dependence or (f1.145.317.269 or c21.739.100.250 or f3.900.100.350)/ct)

L2 411 FILE MEDLINE

L3 208 FILE CAPLUS

L4 331 FILE BIOSIS

L5 427 FILE EMBASE

LEFT TRUNCATION IGNORED FOR '?TRANSFERRIN?' FOR FILE 'WPIDS'

L6 15 FILE WPIDS

LEFT TRUNCATION IGNORED FOR '?TRANSFERRIN?' FOR FILE 'JICST-EPLUS'

L7 4 FILE JICST-EPLUS

TOTAL FOR ALL FILES

L8 1396 (L1 OR ?TRANSFERRIN? OR SIDEROPHILIN? OR (D12.775.124.50.800

OR

D12.776.157.890 OR D12.776.377.715.192.839 OR

D12.776.556.901/CT

)) AND (ALCOHOLISM OR ALCOHOL(2A)(CONSUMP? OR DRINK?) OR

TEMPERA

NCE OR DRUG DEPENDENCE OR (F1.145.317.269 OR C21.739.100.250

OR

F3.900.100.350)/CT)

Left truncation is not valid in the specified search field in the specified file. The term has been searched without left truncation.

Examples: '?TERPEN?' would be searched as 'TERPEN?' and '?FLAVONOID' would be searched as 'FLAVONOID.'

If you are searching in a field that uses implied proximity, and you used a truncation symbol after a punctuation mark, the system may interpret the truncation symbol as being at the beginning of a term.

Prepared by M. Hale 308-4258

Page 2

Implied proximity is used in search fields indexed as single words, for example, the Basic Index.

=> s 18(10a)carbohydrate free

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L2(10A)CARBOHYDRA'
L9 0 FILE MEDLINE
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L3(10A)CARBOHYDRA'
L10 2 FILE CAPLUS
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L4(10A)CARBOHYDRA'
L11 0 FILE BIOSIS
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L5(10A)CARBOHYDRA'
L12 0 FILE EMBASE
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L6(10A)CARBOHYDRA'
L13 2 FILE WPIDS
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L7(10A)CARBOHYDRA'
L14 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES

L15 4 L8(10A) CARBOHYDRATE FREE

=> dup rem 115

PROCESSING COMPLETED FOR L15

L16 2 DUP REM L15 (2 DUPLICATES REMOVED)

=> d cbib abs 1-2 hit

L16 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 1
2000:421411 Document No. 133:40212 Dipstick for **carbohydrate-free transferrin** assay. Sundrehagen, Erling
(Axis-Shield Asa, Norway; Dzieglewska, Hanna). PCT Int. Appl. WO
2000036418 A1 20000622, 50 pp. DESIGNATED STATES: W: AE, AL, AM, AT,
AT

AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK,
DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT,
TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM;
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB,
GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English).
CODEN: PIXXD2. APPLICATION: WO 1999-GB4191 19991210. PRIORITY: GB
1998-27411 19981211.

AB The invention relates to a new dipstick assay for detecting and quantifying the content of an analyte in a sample. The assay is particularly useful for example in the diagnosis and monitoring of alcoholism by the detection of asialo **transferrin** or **carbohydrate free transferrin** (CFT). Thus, provided is a dipstick for detg. the content of a target analyte variant
Prepared by M. Hale 308-4258 Page 3

in a mixt. of analyte variants in a sample, comprising: (a) a sample application zone, (b) a screening zone having an immobilized binding ligand having a binding affinity for a non-target analyte variant or variants, (c) a conjugate zone comprising a detector reagent, (d) a reading zone for detection of said analyte. A dipstick for detn. of CFT in serum had a zone of immobilized Sambucus nigra lectin and ConA above the sample application zone, a detector reagent zone with anti-**transferrin** antibody labeled with blue latex particles, and a reading zone contg. immobilized anti-**transferrin** antibodies. An adsorbent sink pad was at the far end of the dipstick.

TI Dipstick for **carbohydrate-free transferrin**
assay

AB The invention relates to a new dipstick assay for detecting and quantifying the content of an analyte in a sample. The assay is particularly useful for example in the diagnosis and monitoring of alcoholism by the detection of asialo **transferrin** or **carbohydrate free transferrin** (CFT). Thus, provided is a dipstick for detg. the content of a target analyte variant in a mixt. of analyte variants in a sample, comprising: (a) a sample application zone, (b) a screening zone having an immobilized binding ligand having a binding affinity for a non-target analyte variant or variants, (c) a conjugate zone comprising a detector reagent, (d) a reading zone for detection of said analyte. A dipstick for detn. of CFT in serum had a zone of immobilized Sambucus nigra lectin and ConA above the sample application zone, a detector reagent zone with anti-**transferrin** antibody labeled with blue latex particles, and a reading zone contg. immobilized anti-**transferrin** antibodies. An adsorbent sink pad was at the far end of the dipstick.

ST dipstick **carbohydrate free transferrin**;
asialo **transferrin** detection dipstick **alcoholism**

IT **Transferrins**

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(CDT (carbohydrate-deficient **transferrin**); dipstick for **carbohydrate-free transferrin** assay)

IT **Transferrins**

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(asialotransferrins; dipstick for **carbohydrate-free transferrin** assay)

IT Ligands

RL: ARG (Analytical reagent use); DEV (Device component use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(conjugated, with labels, as detector reagents; dipstick for **carbohydrate-free transferrin** assay)

IT Latex

(detector reagent contg. colored particle of, as labels; dipstick for **carbohydrate-free transferrin** assay)

IT Particles

(detector reagent contg., as labels; dipstick for **carbohydrate-free transferrin** assay)

IT Affinity

Blood analysis

Body fluid

Urine analysis

IT (dipstick for carbohydrate-free transferrin assay)

IT Reagents

RL: ARG (Analytical reagent use); DEV (Device component use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

IT (dipstick for carbohydrate-free transferrin assay)

IT Carbohydrates, biological studies

RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)

IT (dipstick for carbohydrate-free transferrin assay)

IT Analytical apparatus

IT (dipstick; dipstick for carbohydrate-free transferrin assay)

IT Transferrins

RL: ARU (Analytical role, unclassified); REM (Removal or disposal); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)

IT (disialo- or monosialo-, removal of; dipstick for carbohydrate-free transferrin assay)

IT Immunoglobulins

RL: ARG (Analytical reagent use); DEV (Device component use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

IT (fragments, to transferrin, labeled; dipstick for carbohydrate-free transferrin assay)

IT Ligands

RL: ARU (Analytical role, unclassified); DEV (Device component use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

IT (immobilized, binding to nontarget analyte variant; dipstick for carbohydrate-free transferrin assay)

IT Antibodies

RL: ARG (Analytical reagent use); DEV (Device component use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

IT (immobilized; dipstick for carbohydrate-free transferrin assay)

IT Antibodies

RL: ARG (Analytical reagent use); DEV (Device component use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

IT (labeled, to transferrin; dipstick for carbohydrate-free transferrin assay)

IT Sialic acids

RL: ARU (Analytical role, unclassified); REM (Removal or disposal); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)

IT (lectin in screening zone binding to; dipstick for carbohydrate-free transferrin assay)

IT Oligosaccharides, analysis

RL: ARU (Analytical role, unclassified); REM (Removal or disposal); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)

(ligand in screening zone binding to; dipstick for **carbohydrate-free transferrin** assay)

IT Alcoholism
(monitoring of; dipstick for **carbohydrate-free transferrin** assay)

IT Agglutinins and Lectins
RL: ARU (Analytical role, unclassified); DEV (Device component use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(of Sambucus nigra, immobilized; dipstick for **carbohydrate-free transferrin** assay)

IT Agglutinins and Lectins
RL: ARU (Analytical role, unclassified); DEV (Device component use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(sialic acid-binding, in screening zone; dipstick for **carbohydrate-free transferrin** assay)

IT 64-17-5, Ethanol, biological studies
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(assessment of consumption of; dipstick for **carbohydrate-free transferrin** assay)

IT 7440-57-5, Gold, biological studies
RL: ARG (Analytical reagent use); DEV (Device component use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(colloid particles, as label; dipstick for **carbohydrate-free transferrin** assay)

IT 11028-71-0D, ConA, immobilized
RL: ARU (Analytical role, unclassified); DEV (Device component use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(dipstick for **carbohydrate-free transferrin** assay)

L16 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 2

1999:42622 Document No. 130:91547 Assay for **carbohydrate-free transferrin**.

Sundrehagen, Erling (Axis Biochemicals) Asa, Norway; Dzieglewska, Hanna, E.). PCT Int. Appl. WO 9900672 A1 19990107, 39 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-GB1875 19980626.

PRIORITY: GB 1997-13559 19970626.

AB The present invention provides a method for the detn. of **carbohydrate-free transferrin** in a body fluid for use in the assessment of alc. **consumption**, said method comprising (a) contacting a sample of said body fluid with a carbohydrate-binding ligand, to bind any carbohydrate or carbohydrate-contg. moieties in said sample to said ligand; (b) sepg. a fraction not binding to said ligand and (c) detg. the content of **transferrin** in said fraction. Also provided are kits for carrying

out such a method.

TI Assay for **carbohydrate-free transferrin**

AB The present invention provides a method for the detn. of **carbohydrate-free transferrin** in a body fluid for use in the assessment of alc. **consumption**, said method comprising (a) contacting a sample of said body fluid with a carbohydrate-binding ligand, to bind any carbohydrate or carbohydrate-contg. moieties in said sample to said ligand; (b) sepg. a fraction not binding to said ligand and (c) detg. the content of **transferrin** in said fraction. Also provided are kits for carrying out such a method.

ST **alcoholism diagnosis carbohydrate free transferrin** detn blood

IT **Transferrins**
RL: ANT (Analyte); BOC (Biological occurrence); BPR (Biological process); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)
(CDT (carbohydrate-deficient **transferrin**); assay for **carbohydrate-free transferrin** as indicator of alcoholism)

IT **Transferrins**
RL: ANT (Analyte); BOC (Biological occurrence); BPR (Biological process); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)
(CFT (carbohydrate-free **transferrin**); assay for **carbohydrate-free transferrin** as indicator of alcoholism)

IT **Alcoholism**
Blood
Blood analysis
Body fluid
Castor bean
Centrifugation
Chromatography
Diagnosis
Elder (Sambucus nigra)
Elder (Sambucus sieboldiana)
Escherichia coli
Filtration
Helicobacter pylori
Immobilization (molecular)
Ion exchange
Liquid chromatography
Maackia amurensis
Nephelometry
Opacifiers
Precipitation (chemical)
Serum (blood)
Sunn hemp (Crotalaria juncea)
Test kits
Turbidimetry
Wheat germ
(assay for **carbohydrate-free transferrin** as indicator of alcoholism)

IT **Sialic acids**
RL: ARU (Analytical role, unclassified); BOC (Biological occurrence); BPR
Prepared by M. Hale 308-4258 Page 7

(Biological process); ANST (Analytical study); BIOL (Biological study);
OCCU (Occurrence); PROC (Process)
(assay for **carbohydrate-free transferrin**
as indicator of alcoholism)

IT Agglutinins
RL: ARU (Analytical role, unclassified); BPR (Biological process); BUU
(Biological use, unclassified); ANST (Analytical study); BIOL (Biological
study); PROC (Process); USES (Uses)
(assay for **carbohydrate-free transferrin**
as indicator of alcoholism)

IT Antibodies
RL: ARU (Analytical role, unclassified); BPR (Biological process); BUU
(Biological use, unclassified); ANST (Analytical study); BIOL (Biological
study); PROC (Process); USES (Uses)
(assay for **carbohydrate-free transferrin**
as indicator of alcoholism)

IT Lectins
RL: ARU (Analytical role, unclassified); BPR (Biological process); BUU
(Biological use, unclassified); ANST (Analytical study); BIOL (Biological
study); PROC (Process); USES (Uses)
(assay for **carbohydrate-free transferrin**
as indicator of alcoholism)

IT Ligands
Proteins (specific proteins and subclasses)
RL: ARU (Analytical role, unclassified); BPR (Biological process); BUU
(Biological use, unclassified); ANST (Analytical study); BIOL (Biological
study); PROC (Process); USES (Uses)
(carbohydrate-binding; assay for **carbohydrate-free**
transferrin as indicator of alcoholism)

IT Immunoassay
(turbidimetric; assay for **carbohydrate-free**
transferrin as indicator of alcoholism)

IT 64-17-5, Ethanol, biological studies
RL: ADV (Adverse effect, including toxicity); BSU (Biological study,
unclassified); BIOL (Biological study)
(assay for **carbohydrate-free transferrin**
as indicator of alcoholism)

IT 11028-71-0, Concanavalin A
RL: ARU (Analytical role, unclassified); BPR (Biological process); BUU
(Biological use, unclassified); ANST (Analytical study); BIOL (Biological
study); PROC (Process); USES (Uses)
(assay for **carbohydrate-free transferrin**
as indicator of alcoholism)

=> s 18(10a)carbohydrate deficien?

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L2(10A)CARBOHYDRA'
L17 260 FILE MEDLINE
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L3(10A)CARBOHYDRA'
L18 145 FILE CAPLUS
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L4(10A)CARBOHYDRA'
L19 245 FILE BIOSIS

Prepared by M. Hale 308-4258

Page 8

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L5(10A)CARBOHYDRA'
L20 251 FILE EMBASE
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L6(10A)CARBOHYDRA'
L21 6 FILE WPIDS
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L7(10A)CARBOHYDRA'
L22 1 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L23 908 L8(10A) CARBOHYDRATE DEFICIEN?

=> s (carbohydrate(w) (free or deficien?)) (5a) (l1 or ?transferrin? or
siderophilin? or (d12.775.124.50.800 or d12.776.157.890 or
d12.776.377.715.192.839 or d12.776.556.901 or d12.776.124.790.223.839) /ct)

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'EFICIEN?') (5A) (L1'
L24 376 FILE MEDLINE
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'EFICIEN?') (5A) (L1'
L25 236 FILE CAPLUS
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'EFICIEN?') (5A) (L1'
L26 459 FILE BIOSIS
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'EFICIEN?') (5A) (L1'
L27 382 FILE EMBASE
LEFT TRUNCATION IGNORED FOR '?TRANSFERRIN?' FOR FILE 'WPIDS'
L28 8 FILE WPIDS
LEFT TRUNCATION IGNORED FOR '?TRANSFERRIN?' FOR FILE 'JICST-EPLUS'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'EFICIEN?') (5A) (L1'
L29 25 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L30 1486 (CARBOHYDRATE(W) (FREE OR DEFICIEN?)) (5A) (L1 OR ?TRANSFERRIN?
OR
D12.7
SIDEROPHILIN? OR (D12.775.124.50.800 OR D12.776.157.890 OR
76.377.715.192.839 OR D12.776.556.901 OR
D12.776.124.790.223.839
)/CT)

The search profile entered contains terms joined by a proximity operator which does not work in the specified field. Some proximity operators work in specific fields. For example, an expression such as 'OLEFINS/CS(L)REACTIONS/CS' cannot be searched as entered if the (L) operator does not apply to the CS field. In such cases, the system does the search in the field you have specified, but changes the proximity operator to 'AND' logic.

To look at the terms, operations, etc., in an L#, enter "DISPLAY QUERY" followed by the L# at an arrow prompt (=>). To see this information for a saved query, enter "ACTIVATE" and the query name, followed by '/Q' at an arrow prompt.

Prepared by M. Hale 308-4258

Page 9

=> s 130(10a) (alcoholism or alcohol(2a) (consump? or drink?) or temperance or drug dependence or (f1.145.317.269 or c21.739.100.250 or f3.900.100.350)/ct)

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L24(10A) (ALCOHOLIS'
L31 260 FILE MEDLINE
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L25(10A) (ALCOHOLIS'
L32 145 FILE CAPLUS
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L26(10A) (ALCOHOLIS'
L33 245 FILE BIOSIS
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L27(10A) (ALCOHOLIS'
L34 251 FILE EMBASE
L35 3 FILE WPIDS
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L29(10A) (ALCOHOLIS'
L36 1 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L37 905 L30(10A) (ALCOHOLISM OR ALCOHOL(2A) (CONSUMP? OR DRINK?) OR
TEMPER
ANCE OR DRUG DEPENDENCE OR (F1.145.317.269 OR C21.739.100.250
OR F3.900.100.350)/CT)

=> s 137 and (asialo or monosialo or trisialo or tetrasialo or pentasialo or
disialo)

L38 8 FILE MEDLINE
L39 14 FILE CAPLUS
L40 7 FILE BIOSIS
L41 6 FILE EMBASE
L42 0 FILE WPIDS
L43 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L44 35 L37 AND (ASIALO OR MONOSIALO OR TRISIALO OR TETRASIALO OR
PENTAS
IALO OR DISIALO)

=> s 144 not 115

L45 8 FILE MEDLINE
L46 13 FILE CAPLUS
L47 7 FILE BIOSIS
L48 6 FILE EMBASE
L49 0 FILE WPIDS
L50 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L51 34 L44 NOT L15

=> dup rem 151

PROCESSING COMPLETED FOR L51
L52 15 DUP REM L51 (19 DUPLICATES REMOVED)

=> d cbib abs 1-15

L52 ANSWER 1 OF 15 MEDLINE DUPLICATE 1
2000403130 Document Number: 20387106. Does **trisialo-transferrin** provide valuable information for the laboratory diagnosis of chronically increased alcohol consumption by determination of **carbohydrate-deficient transferrin**? Dibbelt L. (Institute of Clinical Chemistry, Medical University, D-23538 Luebeck, Germany.) CLINICAL CHEMISTRY, (2000 Aug) 46 (8 Pt 1) 1203-5. Journal code: DBZ. ISSN: 0009-9147. Pub. country: United States. Language: English.

L52 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 2
2000:395294 Document No. 133:130888 Investigation by isoelectric focusing of

the initial **carbohydrate-deficient transferrin** (CDT) and non-CDT **transferrin** isoform fractionation step involved in determination of CDT by the ChronAlcol.D. assay. Hackler, Rolf; Arndt, Torsten; Helwig-Rolig, Angelika; Kropf, Juergen; Steinmetz, Armin; Schaefer, Juergen R. (Zentrum fur Innere Medizin, Abteilung Kardiologie, Philipps-Universitat, Marburg, D-35033, Germany). Clin. Chem. (Washington, D. C.), 46(4), 483-492 (English) 2000. CODEN: CLCHAU. ISSN: 0009-9147. Publisher: American Association for Clinical Chemistry.

AB Background: The introduction of a new set of reagents for the detn. of **carbohydrate-deficient transferrin** (CDT) as a marker of chronic alc. abuse requires an independent evaluation of the analytic specificity of the test. This information is needed for correct interpretation and classification of test results. Methods: Isoelec. focusing on the PhastSystem followed by immunofixation, silver staining, and densitometry was used to validate the initial **transferrin** isoform fractionation step on anion-exchange micro-columns involved in

the ChronAlcoI.D. assay. Results: The in vitro **transferrin** iron load was complete and stable. The CDT and non-CDT **transferrin** fractionation on anion-exchange micro-columns was reliable and reproducible (CV $\leq 10\%$). Except for quant. unimportant traces of **trisialo-Fe2-transferrin** ($<5\%$ of total CDT), only **asialo**-, **mono**-, and **disialo-Fe2-transferrin** were detected in the micro-column eluates ($n = 170$). There was a loss of proportionally similar amts. of **asialo-Fe2-transferrin** (during column rinsing) and **disialo-Fe2-transferrin** (on the anion exchanger). Thus, the peak height ratios for **disialo**- and **asialo-Fe2-transferrin** did not change from >1 (serum) to <1 (eluates) as described for the CDTect assays.

The **transferrin** patterns in the ChronAlcoI.D. eluates were representative of those in serum. **Transferrin** D variants with isoelec. points close to that of **trisialo-Fe2-transferrin** C1 did not cause overdetn. of CDT by the ChronAlcoI.D. test. Conclusions: The initial CDT and non-CDT fractionation step involved in detn. of CDT by the ChronAlcoI.D. assay is efficient for

Prepared by M. Hale 308-4258

Page 11

eliminating non-CDT **transferrins** from serum before quantification of CDT in the final turbidimetric immunoassay. We recommend IEF for validation of other (com.) CDT anal. methods and of odd CDT results.

L52 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2000 ACS

2000:141860 Document No. 132:344172 Improved method for **carbohydrate-deficient transferrin** determination in human serum by capillary zone electrophoresis. Crivellente, F.; Fracasso, G.; Valentini,

R.; Manetto, G.; Riviera, A. P.; Tagliaro, F. (Institute of Forensic Medicine, University of Verona, Verona, Italy). J. Chromatogr., B: Biomed. Sci. Appl., 739(1), 81-93 (English) 2000. CODEN: JCBEP. ISSN: 0378-4347. Publisher: Elsevier Science B.V..

AB **Carbohydrate-deficient transferrin (CDT)** is a reliable marker of chronic or repeated alc. abuse. It indicates a group

of isoforms of human **transferrin (Tf)**, the main iron transport serum protein, deficient in sialic acid residues (**asialo-**, **monosialo-** and **disialo-Tf**) in comparison to the main **isotransferrin** which contains four sialic acid groups (**tetrasialo-Tf**). The aim of the present work was to develop a capillary electrophoretic method suitable for rapid detn. of CDT components in serum. Serum samples (0.1 mL) were satd. with iron by incubation with 10 mM FeCl₃ (2 .mu.l) and 500 mM NaHCO₃ (3 .mu.l) for 30 min, then dild. 1:10 in water and injected by pos. pressure (0.5 p.s.i. for 10 s). Sepn. was performed with a capillary zone electrophoretic method using bare fused-silica capillaries (57 cm.times.20 .mu.m I.D.)

and

a buffer composed of 100 mM sodium tetraborate adjusted with 6 M HCl to

pH

8.3 added with 1.5 mM diaminobutane. Applied voltage was 20 kV and temp. 25.degree.. Detection was by UV absorption at 200 nm wavelength. Under the described conditions, **asialo-**, **monosialo-**, **disialo-**, **trisialo-** and **tetrasialo-transferrin** were baseline sepd. The limit of detection (signal-to-noise ratio of 2) was about 0.3% for **disialo-Tf**, and 0.5% of **trisialo-Tf**, expressed as percentages of the **terasialo-Tf** peak area. Day-to-day RSDs of relative migration times were .1toreq.0.2%. Quantitation showed day-to-day RDSs .1toreq.6.9% and .1toreq.10.9% for **disialo-** and **trisialo-Tf**, resp. The results from 79 control subjects, including social drinkers, and 23 alcoholics showed **disialo-** and **trisialo-Tf** significantly increased in patients (P<0.0001 and <0.01, resp.). A clear interference from **trisialo-Tf** in an immunoassay for CDT was demonstrated. The present method is suitable for confirmation of CDT immunoassays by independent technique.

L52 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2000 ACS

1999:516842 Document No. 131:155457 Experience with the examination of **carbohydrate-deficient transferrin**. Stejskal, David; Vavrouskova, J.; Frankova, M.; Jedelsky, L.; Horalik, D.; Pastorkova, R. (Oddeleni Laboratorni Mediciny, Nemocnice Sternberk, Sternberk, 78516, Czech Rep.). Vnitr. Lek., 45(6), 347-352 (Czech) 1999. CODEN: VNLEAH. ISSN: 0042-773X. Publisher: Ceska Lekarska Spolecnost J. Ev. Purkyne.

AB **Carbohydrate-deficient blood serum transferrin**
(CDT) is considered a useful indicator of alc. abuse. There is a no. of methods for the CDT status assessment. The most frequent clin. assessment

uses the percentage of CDT in total **transferrin**. We assessed CDT by the Boehringer (CDT-BM) and Sanqui BioTech (CDT-SB) homogeneous immunoanal. in 49 alc. patients, including 16 who admitted alc. abuse >60 g alc. more than 4-times per wk. The %CDT detd. by the CDT-BM method was higher than with the CDT-SB. After classification of the patients into 2 subgroups based on alc. intake the subgroups differed only in the values of CDT-SB and CDT-BM. In the subgroup of patients with alc. abuse we found relations between CDT-MB and indicators of hepatic lesions. CDT-SB showed an assocn. only with the blood aspartate transaminase activity. This may suggest a greater specificity of CDT-SB. The values of **gamma**-glutamyl transferase activity and the mean corpuscular vol. were independent of CDT in subjects with alc. abuse. In patients who negated alc. intake the CDT-SB found a gender difference probably because the CDT-SB method (unlike CDT-BM) detects only **asialo**, **monosialo**, and **disialo** isoforms of **transferrin** and women have higher levels of **monosialo** forms. The CDT-SB method had almost abs. specificity and sensitivity. Compared to the older

CDT-BM method, with CDT-SB we did not find any false increases in patients with hepatopathy symptoms or false neg. results. The described methodol. innovation may facilitate differential diagnosis of various diseases.

L52 ANSWER 5 OF 15 MEDLINE

2000247948 Document Number: 20247948. [CDT (desialylated **transferrin**)--a new biochemical marker of alcohol abuse]. CDT (desialowana transferyna)--nowy biochemiczny marker naduzywania alkoholu. Chrostek L; Szmiltkowski M. (Zakladu Diagnostyki Biochemicznej AM w Bialymstoku.) PSYCHIATRIA POLSKA, (1999 Mar-Apr) 33 (2) 189-201. Journal code: QBJ. ISSN: 0033-2674. Pub. country: Poland. Language: Polish.

AB Serum concentration of **carbohydrate-deficient transferrin** (CDT) is used for laboratory diagnosis of chronic alcohol abuse. Several earlier studies reported sensitivities of 90% or above for CDT, with a specificity of 90-100%, although other investigators

found lower sensitivities. In general, CDT has been reported to be highly specific (92%) and relatively sensitive (80%) for the detection and monitoring of **alcoholism**. There are no correlation between CDT concentration and gamma-GT activity. Any alteration in serum total **transferrin** concentration markedly decreases the CDT assay specificity. This should be considered when interpreting the assay results

in patients with elevated serum **transferrin**. There are differences between the CDT isoforms (**asialo-Tf** and **monosialo-Tf**) in males and females relative to **alcohol consumption**. **Alcohol consumption** increases the levels of **asialo-Tf** and **monosialo-Tf** in women more strongly than in men. Sensitivity of CDT assay is also related to age of patients. There is a significantly higher sensitivity of CDT in patients above 40 years of age as compared to younger patients. The measurement of **carbohydrate-deficient transferrin** may be used as a marker of excessive alcohol abuse in patients with liver diseases

Prepared by M. Hale 308-4258

Page 13

(also in cirrhosis). The specificity of CDT in patients with non-alcoholic liver disease was consistently higher than that of gamma-GT (80% vs 60%). Disulfiram therapy during detoxification does not influence the serum level of CDT.

L52 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2000 ACS
1998:800076 Document No. 130:34380 An improved method for diagnosing alcohol abuse. Sillanaukee, Pekka (Pharmacia & Upjohn Diagnostics Ab, Swed.). PCT Int. Appl. WO 9854576 A1 19981203, 34 pp. DESIGNATED STATES: W: JP, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1998-SE1016 19980528.

PRIORITY: SE 1997-2020 19970529.
AB A method for diagnosing alc. abuse of an individual is characterized in that the levels of **carbohydrate-deficient transferrins** (marker 1) and at least one liver status marker (marker 2) are measured in a body fluid sample whereafter the levels for the markers are weighted to a common value according to a formula giving a better sensitivity and/or specificity than obtained for either or both of the markers, said value then being correlated to alc. abuse.

L52 ANSWER 7 OF 15 MEDLINE DUPLICATE 3
1999085956 Document Number: 99085956. Optimized determination of **carbohydrate-deficient transferrin** isoforms in serum by capillary zone electrophoresis. Tagliaro F; Crivellente F; Manetto G; Puppi I; Deyl Z; Marigo M. (Institute of Forensic Medicine, University of Verona, Italy.. ftmed1@borgoroma.univ.it) .

ELECTROPHORESIS, (1998 Nov) 19 (16-17) 3033-9. Journal code: ELE. ISSN: 0173-0835. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.
AB **Carbohydrate deficient transferrin (CDT)** is one of the most reliable markers of chronic alcohol abuse. It consists of a group of minor isoforms of human **transferrin** (the main iron transport serum protein) deficient in sialic acid groups (**asialo**, **monosialo** and **disialo**) with a PI > 5.7, while the main **isotransferrin (tetrasialo)** has a PI of 5.4. The aim of the present work was to develop a capillary electrophoretic method to determine CDT in serum, suitable for routine use as a confirmatory technique of the current screening methods based on immunoassays. Serum samples (0.5 mL) were saturated with iron by incubation with 10 mM FeCl₃ (9 microL) and 500 mM NaHCO₃ (12 microL) for 30 min, then diluted 1/10 in water and injected by positive pressure (0.5 psi for 10 s). Separation was performed with a capillary zone electrophoretic method using bare fused-silica capillaries (20 microm ID, 37 cm in length) and a buffer composed of 100 mM sodium tetraborate adjusted with boric acid to pH 8.3. Applied voltage was 10 kV and temperature 25 degrees C. Detection was by UV absorption at 200 nm wavelength. Under the described conditions, **asialo**-, **monosialo**-, **disialo**-, **trisialo**- and **tetrasialo-transferrin** were separated in human serum. The limit of detection (signal-to-noise ratio of 2) was about 0.3% for **disialo-transferrin**, and 0.4% of

Prepared by M. Hale 308-4258

trisialo-transferrin, expressed as percentages of the terasialo-transferrin peak area. Relative standard deviations (RSD) of absolute migration times were < 1%, while RSD of relative migration times (on the basis of **tetasialo-transferrin**) were < 0.1%. Intra-day and day-to-day peak quantitation precision studies showed RDS ranging from 4 to 9% and from 13 to 24% for **disialo-** and **trisialo-transferrin**, respectively. The results from 30 control subjects, including social drinkers, and 13 alcoholics showed **disialo-** and **trisialo-transferrin** significantly increased in patients by a factor of about 4.5 (P < 0.0001).

L52 ANSWER 8 OF 15 MEDLINE

DUPLICATE 4

1998209925 Document Number: 98209925. Validation by isoelectric focusing of the anion-exchange **isotransferrin** fractionation step involved in determination of **carbohydrate-deficient transferrin** by the CDTect assay. Arndt T; Hackler R; Kleine T O; Gressner A M. (Abteilung fur Klinische Chemie und Zentrallaboratorium, Philipps-Universitat, Marburg, Germany.. bioscientia@t-online.de) . CLINICAL CHEMISTRY, (1998 Jan) 44 (1) 27-34. Journal code: DBZ. ISSN: 0009-9147. Pub. country: United States. Language: English.

AB

Serum concentration of **carbohydrate-deficient transferrin** (CDT) is used for laboratory diagnosis of chronic alcohol abuse. Using isoelectric focusing for validation of the initial **isotransferrin** fractionation step involved in the determination of CDT by the CDTect assay, we found a complete in vitro iron saturation of **transferrin** and sufficient stability of the **transferrin** iron load during column passage; effective separation of non-CDT-**isotransferrins** and CDT-**isotransferrins** at the microcolumns; partial coelution of **trisialo-Fe2-transferrin**, which did not significantly affect CDT measurement; partial retention of CDT-**isotransferrins**, especially **disialo-Fe2-transferrin**, which may cause falsely negative results for CDT at the upper reference limits; good precision of the **isotransferrin** fractionation step; and no significant effects of low concentrations of serum protein and **transferrin**. We strongly urge standardization of CDT analysis and suggest isoelectric focusing for validation of CDT analysis methods and verification of odd results.

L52 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2000 ACS

DUPLICATE 5

1997:750017 Document No. 128:1015 Analysis of **carbohydrate deficient transferrin** by capillary zone electrophoresis.

Prasad, Rajani; Stout, Robert L.; Coffin, David; Smith, James (Clinical Reference Laboratory, Lenexa, KS, 66215, USA). Electrophoresis, 18(10), 1814-1818 (English) 1997. CODEN: ELCTDN. ISSN: 0173-0835. Publisher: Wiley-VCH Verlag GmbH.

AB

A capillary zone electrophoresis was reported to sep. the various sialylated isoforms of **transferrin**. The sepn. is carried out under nondenaturing conditions and at basic pH. Under these conditions, **transferrin** exhibits 2 major and 3 minor peaks. Blood plasma samples from a population consuming varying amts. of alc. at different intervals were studied. A cut-off value of 3% **carbohydrate deficient transferrin** (CDT: **disialo, monosialo, and asialo transferrin**), results in a clin. sensitivity of 88% in a population consuming at least 70 g/day

Prepared by M. Hale 308-4258

Page 15

alc. for a min. of 2 wk. The sensitivity dropped in a population consuming less than 70 g/day. This confirms previous reports of CDT as a specific marker for significant and chronic use of alc. Capillary electrophoresis offers an alternative method with respect to anal. time and throughput in the clin. lab.

L52 ANSWER 10 OF 15 MEDLINE

DUPLICATE 6

1998099372 Document Number: 98099372. **Transferrin isoform distribution: gender and alcohol consumption.**
Martensson O; Harlin A; Brandt R; Seppa K; Sillanaukee P. (Pharmacia & Upjohn AB, Diagnostics, Alcohol Related Diseases, Uppsala, Sweden.) **ALCOHOLISM, CLINICAL AND EXPERIMENTAL RESEARCH**, (1997 Dec) 21 (9) 1710-5. Journal code: 35X. ISSN: 0145-6008. Pub. country: United States.

Language:

English.

AB **Transferrin (Tf)** has different isoforms based on the degree of sialylation of its two N-linked oligosaccharide chains. The least sialylated isoforms of Tf; with 0 (**asialo Tf**), 1 (**monosialo Tf**), and 2 (**disialo Tf**) sialic acids are referred to as **carbohydrate-deficient transferrin** (CDT). CDT has been reported to be a specific and sensitive marker for the detection and monitoring of alcohol abuse. However, the possible differences between the three CDT isoforms in males and females relative to **alcohol consumption** has not been known. The present study included 82 males (M) and 43 females (F) with well documented drinking habits. The Tf isoforms were separated by FPLC and measured by RIA in the collected fractions, as well as by a commercially available method (CDTect RIA). The results were expressed as relative values and absolute values. Female low consumers compared to

male

low consumers had higher levels of **asialo Tf** ($p < 0.01$) and **monosialo Tf** ($p < 0.01$), but not of **disialo Tf** or sum of **asialo, monosialo, and disialo Tf**. Male high consumers and chronic consumers compared to male low consumers had 53%

and

219% higher levels of **asialo Tf**, 4% and 28% higher **monosialo Tf**, 57% and 148% higher **disialo Tf**, and 48% and 134% higher sum of CDT isoforms, respectively. The corresponding increases in females were for **asialo Tf** 68% and 249%, for **monosialo Tf** 36% and 58%, for **disialo Tf** 54% and 225%, and for sum of CDT isoforms 52% and 192%, respectively. For both genders, total Tf, **trisialo Tf**, and the levels of more sialylated **transferrin** isoforms were constant when comparing the consumption groups. Results expressed as relative values and absolute values were in good agreement. In conclusion, the present study indicates that **alcohol consumption** strongly increases the levels of **asialo Tf** and **disialo Tf** and slightly increases the level of **monosialo Tf**. However, women had higher **asialo Tf** and **monosialo Tf** levels than men. **Alcohol consumption** does not increase **trisialo** or more sialylated Tf subfractions. Expressing the CDT results as absolute or relative

values

made no obvious difference in diagnostic efficiency.

L52 ANSWER 11 OF 15 MEDLINE

DUPLICATE 7

97221546 Document Number: 97221546. **Quantification of carbohydrate** Prepared by M. Hale 308-4258 Page 16

-deficient transferrin by ion-exchange chromatography with an enzymatically prepared calibrator. Renner F; Kanitz R D.
(Institut fur Klinische Chemie, Medizinische Universitat zu Lubeck, Germany.) CLINICAL CHEMISTRY, (1997 Mar) 43 (3) 485-90. Journal code: DBZ. ISSN: 0009-9147. Pub. country: United States. Language: English.
AB The current HPLC method for the determination of carbohydrate-deficient transferrin (CDT) yields ratios of CDT isoforms in relation to total transferrin, whereas the use of absolute concentrations obtainable in routine analysis by RIA and the reference ranges based here-upon is more convenient. We describe a modified HPLC method that likewise gives absolute CDT concentrations by using a calibrator prepared by treatment of transferrin with neuraminidase. Separation of isoforms could be improved and analysis time reduced to approximately 2 h. Iron saturation proved stable during chromatography. In contrast to a commercial RIA, the cheaper and more time-saving HPLC method excludes erroneous results caused by aged samples or genetic transferrin variants and enables the determination of asialo- and disialotransferrin. Both methods showed comparable precision and correlated with each other ($y = 1.76 + 0.27x$; $Sy[\text{symbol: see text}]x = 5.38$); for the HPLC method precision was 1.3-9.8% (within assay) and 6.2-10.6% (between assay). The clinical evaluation with a cutoff concentration of 80 mg/L resulted in a diagnostic specificity of 100% and a sensitivity of 82.5%.

L52 ANSWER 12 OF 15 MEDLINE DUPLICATE 8
97033627 Document Number: 97033627. Should tri-sialo-transferrins be included when calculating carbohydrate-deficient transferrin for diagnosing elevated alcohol intake?. Heggli D E; Aurebakk A; Granum B; Westby C; Lovli T; Sundrehagen E. (Axis Biochemicals AS, Oslo, Norway.) ALCOHOL AND ALCOHOLISM, (1996 Jul) 31 (4) 381-4. Journal code: AAL. ISSN: 0735-0414. Pub. country: ENGLAND: United Kingdom.

Language: English.
AB CDT (carbohydrate-deficient transferrin) has been identified as a specific marker for chronically elevated alcohol consumption. We investigated the sensitivity and accuracy of using relative concentrations of different isotransferrins in serum for diagnosis of chronically elevated alcohol consumption. The different transferrin variants (isoforms) were quantified by HPLC. Including the trisialo-transferrin fraction into the definition of %CDT resulted in an increased accuracy in the detection of chronically elevated alcohol intake in a study among 17 heavy drinkers, 25 healthy individuals with moderate alcohol consumption and nine total abstainers. The results also suggest that desialylation of transferrin is a gradually continuing process, rather than one leading to a single end-result separating asialo-, mono- and disialo-transferrins from trisialo-, tetrasialo-, pentasialo- and higher sialo-transferrins.

L52 ANSWER 13 OF 15 MEDLINE DUPLICATE 9
95150262 Document Number: 95150262. Comparison of different methods for Prepared by M. Hale 308-4258 Page 17

detecting **carbohydrate-deficient transferrin**

. Sillanaukee P; Lof K; Harlin A; Martensson O; Brandt R; Seppa K. (Biomedical Research Center, Alko Ltd., Helsinki, Finland.) **ALCOHOLISM, CLINICAL AND EXPERIMENTAL RESEARCH**, (1994 Oct) 18 (5) 1150-5. Journal code: 35X. ISSN: 0145-6008. Pub. country: United States. Language: English.

AB Different methods for detecting **carbohydrate-deficient transferrin** (CDT) were compared. In addition, their efficiency for detecting alcohol abuse among men not having clinical evidence of liver disease was studied in controls (n = 26), weekend (n = 16) and daily (n = 12) heavy drinkers, and alcoholics (n = 28). Comparisons were made

between

anion-exchange separation of iron-saturated **transferrin** (Tf) by microcolumns (CDTect) and by the Fast Protein Liquid Chromatography

(FPLC%)

and FPLC-MG), followed by double-antibody radioimmunoassay of collected fractions. Tf fractions with $pI > 5.7$ were also measured by two different isoelectric focusing (IEF) methods, followed by immunofixation (SA-IEF-CDT and IEF-CDT-TOT), the latter method being used also for detection of **asialotransferrin** (IEF-CDT-AS). The cut-off was 20 units/liter for CDTect, 4.4% of total Tf for SA-IEF-CDT, and the mean ± 2 sd of the control group for FPLC-MG (as mg/liter of Tf), FPLC-%, IEF-CDT-TOT, and IEF-CDT-AS (all as percentage of Tf). The overall accuracies (combining sensitivity and specificity) for detecting heavy drinkers of CDTect, FPLC (mg/liter), FPLC (%), SA-IEF-CDT, IEF-CDT-TOT, and IEF-CDT-AS were 63%, 59%, 61%, 74%, 57%, and 63%, respectively; for detecting alcoholics, 87%, 83%, 81%, 89%, 37%, and 76%, respectively. In conclusion, the methods were in rather good agreement with each other. Diagnostic characteristics among heavy drinkers and correlations between methods differed slightly, probably depending on the ability of different methods to separate and detect **asialo-, monosialo-, and disialotransferrin**. (ABSTRACT TRUNCATED AT 250 WORDS)

L52 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2000 ACS

1993:227670 Document No. 118:227670 Desialylated **transferrin**. A

new approach in diagnosis of **alcoholism**. Wedig, M. P. (Klin. Eichholz, Bad Waldliesborn, Germany). Mol. Cell Biol. Liver Fibrogenesis,

Proc. Int. Falk Symp., 548-50. Editor(s): Gressner, A. M.; Ramadori, G. Kluwer: Dordrecht, Neth. (English) 1992. CODEN: 58ZZAF.

AB Recently, desialylated **transferrin** (dTf, also known as **carbohydrate-deficient transferrin**) and the mitochondrial isoenzyme of aspartate aminotransferase have been proposed as being more sensitive and specific biochem. markers of alc. abuse than are conventional lab. tests. Abnormal **transferrin** variants with less sialic acid content were found in the serum of alc. subjects.

L52 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2000 ACS

1994:47907 Document No. 120:47907 Sialic acid-deficient **transferrin**

: a very attractive biological marker related to chronic **alcoholism**. Renversez, J. C.; Alzieu, C.; Vernet, M. (Lab. Biochim. A, CHRU de Grenoble, Grenoble, 38043, Fr.). Ann. Biol. Clin., 50(1), 1-7 (French) 1992. CODEN: ABCLAI. ISSN: 0003-3898.

AB Sialic acids-deficient **transferrins**: a very attractive biol. marker related to chronic **alcoholism**. Chronic **alcoholism** may induce modifications of plasma **transferrin**

Prepared by M. Hale 308-4258

Page 18

: alc. modifies the content of its branched oligosaccharides. The abnormal **transferrin** contains reduced amts. of sialic acids, constituting its terminal trisaccharides biantennary chains. Plasma levels of partly deficient or **asialotransferrin** (**carbohydrate-deficient transferrin** or CDT) increase in chronically drinkers. A pos. correlation is obtained between the plasmatic concn. of CDT and the amt. of ingested alc. Positivity and sensitivity of CDT are superior to those of other usual biol. parameters. The CDT quantitation may be used for the detection and the follow-up of alc. **drinkers** to evaluate the degree of intoxication, and during the period of withdrawal.

=> s 137 not 144

L53 252 FILE MEDLINE
L54 131 FILE CAPLUS
L55 238 FILE BIOSIS
L56 245 FILE EMBASE
L57 3 FILE WPIDS
L58 1 FILE JICST-EPLUS

TOTAL FOR ALL FILES

L59 870 L37 NOT L44

=> s 159 not 115

L60 252 FILE MEDLINE
L61 130 FILE CAPLUS
L62 238 FILE BIOSIS
L63 245 FILE EMBASE
L64 1 FILE WPIDS
L65 1 FILE JICST-EPLUS

TOTAL FOR ALL FILES

L66 867 L59 NOT L15

=> s 166 and (bind? ligand or lectin?)

L67 4 FILE MEDLINE
L68 2 FILE CAPLUS
L69 2 FILE BIOSIS
L70 1 FILE EMBASE
L71 0 FILE WPIDS
L72 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES

L73 9 L66 AND (BIND? LIGAND OR LECTIN?)

=> dup rem 173

PROCESSING COMPLETED FOR L73

L74 6 DUP REM L73 (3 DUPLICATES REMOVED)

=> d cbib abs 1-6

L74 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2000 ACS

2000:384553 Document No. 133:28245 Diagnosis of human glycosylation disorders. Marth, Jamey D.; Freeze, Hudson H. (The Regents of the University of California, USA; The Burnham Institute). PCT Int. Appl. WO 2000033076 A1 20000608, 95 pp. DESIGNATED STATES: W: AE, AL, AM, AT,

AU,

AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US28591 19991201. PRIORITY: US 1998-PV110671 19981202; US 1998-PV113680 19981221; US 1998-PV114174 19981230.

AB This invention provides methods and kits for use in diagnosing genetically

transmitted diseases that are assocd. with deficiencies in glycosylation of glycoconjugates such as glycoproteins, glycolipids, and proteoglycans. The methods and kits are also useful for monitoring the course of treatment of diseases that are assocd. with glycosylation disorders.

Blood from patient with **carbohydrate-deficient**

glycoprotein syndrome (CDGS) type II did not bind to E-PHA (erythroagglutinin of Phaseolus vulgaris) or to L-PHA (leucoagglutinin of

Phaseolus vulgaris) lectins but showed increased binding to ConA lectin. Mouse models were constructed having defects in certain enzyme genes and the models were studied.

L74 ANSWER 2 OF 6 BIOSIS COPYRIGHT 2000 BIOSIS

2000:374337 Document No.: PREV200000374337. Glycobiochemical and clinical similarity between patients with alcoholic liver disease and **carbohydrate-deficient** glycoprotein syndrome (CDGS).

Yamauchi, M. (1); Inoue, T. (1); Searashi, Y. (1); Nishikawa, F. (1); Ohata, M. (1); Toda, G. (1); Ohkawa, K. (1) Department of Internal Medicine, Jikei University School of Medicine, Tokyo Japan. Alcoholism Clinical and Experimental Research, (May, 2000) Vol. 24, No. 5

Supplement,

pp. 205A. print. Meeting Info.: Tenth Congress of the International Society for Biomedical Research on Alcoholism Yokohama, Japan July 02-08, 2000 Research Society on Alcoholism. ISSN: 0145-6008. Language: English. Summary Language: English.

L74 ANSWER 3 OF 6 MEDLINE

DUPLICATE 1

1999412174 Document Number: 99412174. Determination of **carbohydrate-deficient** transferrin separated by lectin affinity chromatography for detecting chronic alcohol abuse. Yoshikawa K; Umetsu K; Shinzawa H; Yuasa I; Maruyama K; Ohkura T; Yamashita K; Suzuki T. (Department of Forensic Medicine, Yamagata University School of Medicine, Japan.) FEBS LETTERS, (1999 Sep 17) 458 (2) 112-6. Journal code: EUH. ISSN: 0014-5793. Pub. country: Netherlands. Language: English.

AB **Carbohydrate-deficient** transferrin (CDT) has been established as a valuable biological marker for detecting chronic alcohol abuse. To improve the diagnostic efficiency, we studied new CDT determination procedures involving the use of lectin affinity

Prepared by M. Hale 308-4258

Page 20

chromatography with *Allomyrina dichotoma* agglutinin (allo A) and *Trichosanthes japonica* agglutinin I (TJA-I) to isolate the CDT isoforms CDT-allo A and CDT-TJA, respectively. These procedures, based on detection of the CDT-allo A and CDT-TJA isoforms in sera, showed high sensitivity (100% and 98%, respectively) and high specificity (93% and 85%, respectively). These results demonstrate that the new procedures involving the use of lectin affinity chromatography are more useful for isolating markers in the CDT test than the conventional charge-based separation method.

L74 ANSWER 4 OF 6 MEDLINE

1998207678 Document Number: 98207678. Identification of **carbohydrate deficient transferrin** forms by MALDI-TOF mass spectrometry and lectin ELISA *Biochim Biophys Acta* 1998 Aug 24;1381(3):356. Peter J; Unverzagt C; Engel W D; Renauer D; Seidel C; Hosel W. (Institut fur Organische Chemie und Biochemie, Technische Universitat Munchen, Garching, Germany.) *BIOCHIMICA ET BIOPHYSICA ACTA*, (1998 Mar 12) 1380 (1) 93-101. Journal code: AOW. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB **Transferrin** was isolated from sera of patients with severe alcohol abuse and from control sera by affinity chromatography using an immobilized polyclonal antibody from sheep, followed by gel filtration. The purified **transferrin** was then separated by MonoQ chromatography. Compared to the controls, sera from heavy alcohol consumers showed two additional **transferrin** peaks, eluting earlier than the three main **transferrin** forms present in all sera. Further analysis of the isolated **transferrin** forms by matrix assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF-MS) and enzyme linked immunosorbent assay with different digoxigenylated lectins (lectin ELISA) revealed that the main **carbohydrate deficient transferrin** (CDT) forms are lacking either one or both of the N-Glycan chains.

L74 ANSWER 5 OF 6 MEDLINE

97139638 Document Number: 97139638. Microheterogeneity with concanavalin A affinity of serum **transferrin** in patients with alcoholic liver disease. Inoue T; Yamauchi M; Toda G; Ohkawa K. (Tikei University School of Medicine, Tokyo, Japan.) *ALCOHOLISM, CLINICAL AND EXPERIMENTAL RESEARCH*, (1996 Dec) 20 (9 Suppl) 363A-365A. Journal code: 35X. ISSN: 0145-6008. Pub. country: United States. Language: English.

AB Microheterogeneity of **transferrin** (Tf) with concanavalin A (ConA) affinity was investigated by sensitive lectin-affinity electrophoresis and antibody-affinity blotting technique of sera obtained from patients with alcoholic liver disease (ALD) and normal subjects. Serum Tf was separated by ConA into three bands-a strongly ConA-reactive major band (C1), a weakly reactive minor band (C2), and a non-reactive trace band (C3). The C3 fraction was significantly increased in patients with ALD before alcohol abstinence, compared with normal subjects and patients with ALD after 4 weeks of abstinence. Furthermore, a significant correlation was found between the C3 fraction and serum **carbohydrate-deficient transferrin** or gamma-glutamyl-transpeptidase. These results indicate that the microheterogeneity of serum Tf in patients with ALD may be a more complex

abnormality of elongation and processing on the glycans than merely a loss of terminal sialic acids. Determination of the C3 fraction is a useful marker for ALD.

L74 ANSWER 6 OF 6 MEDLINE

DUPLICATE 2

96176959 Document Number: 96176959. New alterations of serum glycoproteins in alcoholic and cirrhotic patients revealed by high resolution two-dimensional gel electrophoresis. Gravel P; Walzer C; Aubry C; Balant

L

P; Yersin B; Hochstrasser D F; Guimon J. (Clinical Research Unit, Psychiatric University Institutions of Geneva, Switzerland.) BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1996 Mar 7) 220 (1) 78-85. Journal code: 9Y8. ISSN: 0006-291X. Pub. country: United States.

Language:

English.

AB Plasma protein are synthesized and secreted by the liver. Several reports have shown that excessive consumption of ethanol interferes with the hepatic protein synthesis and/or secretion. This study was undertaken to identify the plasma/serum proteins altered in two groups of patients with different alcohol-related diseases: actively drinking alcoholic patients group without liver disease and alcohol cirrhotic patients group. Two-dimensional gel electrophoresis was used to separate proteins with high resolution. Proteins were detected by silver staining and glycoproteins were specifically visualized and analyzed after lectin blotting followed by chemiluminescence detection. Different protein alterations were identified in each group of patients. In the alcoholic group, two new glycosylation modifications of serum proteins were identified. An abnormal microheterogeneity of haptoglobin and alphal-antitrypsin was detected in the serum of all alcoholic patients.

We

also characterized by two-dimensional gel electrophoresis the carbohydrate deficient transferrin. The modifications of haptoglobin, alphal-antitrypsin and **transferrin** present a similar change of charge and molecular weight in the two-dimensional gel electrophoresis pattern. These qualitative estimations support the hypothesis of a general mechanism of liver glycosylation alteration of serum proteins induced by excessive **alcohol consumption**. The immunoglobulin alterations were easily visualized and identified for the cirrhotic and the alcoholic patients. And finally, the decrease of haptoglobin and albumin spots for cirrhotic patients was confirmed.

=> s 166 not 173

L75 248 FILE MEDLINE

L76 128 FILE CAPLUS

L77 236 FILE BIOSIS

L78 244 FILE EMBASE

L79 1 FILE WPIDS

L80 1 FILE JICST-EPLUS

TOTAL FOR ALL FILES

L81 858 L66 NOT L73

Prepared by M. Hale 308-4258

Page 22

=> s (sambuc? or maack? or escherchia or helicobacter or ricin? or crotalar?
or anti sialic acid) (5a) lectin and 181

L82 0 FILE MEDLINE
L83 0 FILE CAPLUS
L84 0 FILE BIOSIS
L85 0 FILE EMBASE
L86 0 FILE WPIDS
L87 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES

L88 0 (SAMBUC? OR MAACK? OR ESCHERCHIA OR HELICOBACTER OR RICIN? OR
CROTALAR? OR ANTI SIALIC ACID) (5A) LECTIN AND L81

=> s 181 and blood

L89 224 FILE MEDLINE
L90 79 FILE CAPLUS
L91 87 FILE BIOSIS
L92 132 FILE EMBASE
L93 1 FILE WPIDS
L94 1 FILE JICST-EPLUS

TOTAL FOR ALL FILES

L95 524 L81 AND BLOOD

=> s 181 and body fluid

L96 0 FILE MEDLINE
L97 2 FILE CAPLUS
L98 1 FILE BIOSIS
L99 0 FILE EMBASE
L100 1 FILE WPIDS
L101 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES

L102 4 L81 AND BODY FLUID

=> s (195 or 1102) and (determ? or detm or method)

L103 109 FILE MEDLINE
L104 49 FILE CAPLUS
L105 57 FILE BIOSIS
L106 68 FILE EMBASE
L107 1 FILE WPIDS
L108 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES

L109 284 (L95 OR L102) AND (DETERM? OR DETM OR METHOD)

=> s 1109 and (separat? or precipit? or centrifug? or filt? or chromatograph?)

L110 31 FILE MEDLINE
L111 18 FILE CAPLUS
L112 14 FILE BIOSIS

Prepared by M. Hale 308-4258

Page 23

L113 19 FILE EMBASE
L114 0 FILE WPIDS
L115 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES

L116 82 L109 AND (SEPARAT? OR PRECIPIT? OR CENTRIFUG? OR FILT? OR
CHROMA
TOGRAPH?)

=> s 1116 and (turbidomet? or nephelomet?)

L117 1 FILE MEDLINE
L118 1 FILE CAPLUS
L119 0 FILE BIOSIS
L120 1 FILE EMBASE
L121 0 FILE WPIDS
L122 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES

L123 3 L116 AND (TURBIDOMET? OR NEPHELOMET?)

=> s 1116 and kit

L124 7 FILE MEDLINE
L125 2 FILE CAPLUS
L126 5 FILE BIOSIS
L127 5 FILE EMBASE
L128 0 FILE WPIDS
L129 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES

L130 19 L116 AND KIT

=> s 1123 or 1130

L131 8 FILE MEDLINE
L132 3 FILE CAPLUS
L133 5 FILE BIOSIS
L134 6 FILE EMBASE
L135 0 FILE WPIDS
L136 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES

L137 22 L123 OR L130

=> dup rem 1137

PROCESSING COMPLETED FOR L137
L138 10 DUP REM L137 (12 DUPLICATES REMOVED)

=> d 1-10 cbib abs;s 1109 and assay

L138 ANSWER 1 OF 10 MEDLINE DUPLICATE 1
2000260921 Document Number: 20260921. Biological markers of
alcoholism with respect to genotypes of low-Km aldehyde
Prepared by M. Hale 308-4258

dehydrogenase (ALDH2) in Japanese subjects. Nomura F; Itoga S; Tamura M; Harada S; Iizuka Y; Nakai T. (Institute of Clinical Medicine, Tsukuba University, Tokyo, Japan.) ALCOHOLISM, CLINICAL AND EXPERIMENTAL RESEARCH, (2000 Apr) 24 (4 Suppl) 30S-33S. Journal code: 35X. ISSN: 0145-6008. Pub. country: United States. Language: English.

AB BACKGROUND: Although the mutant low-Km acetaldehyde dehydrogenase (ALDH2) allele (ALDH2(2)) with reduced capacity to metabolize acetaldehyde offers biological protection against **alcoholism** and subsequent alcohol-induced organ damage in many individuals, a significant proportion

of individuals with heterozygote of the normal and mutant ALDH2 gene (ALDH2(1)/2(2)) consume excessive amounts of alcohol. Indeed, it has been postulated that habitual drinkers with ALDH2(1)/2(2) may be at a higher risk for alcoholic liver disease than those with ALDH2(1)/2(1). In this study, we determined how representative biological markers of **alcoholism** (gamma-glutamyltransferase [GGT], **carbohydrate**-deficient **transferrin** [CDT], and the mean corpuscular volume of erythrocytes [MCV]) differ with respect to the ALDH2 genotypes in Japanese habitual drinkers. METHODS: We obtained genomic DNA samples from 227 Japanese men with various drinking habits. ALDH2 genotypes were determined by allele-specific polymerase chain reaction. GGT, CDT, and MCV were determined and compared between ALDH2(1)/2(1) and ALDH2(1)/2(2) habitual drinkers who consumed more than 66 g of alcohol per day for more than 5 years. We measured CDT by anion-exchange **chromatography** followed by turbidity immunoassay by using a commercially available assay kit (Axis %CDT TIA).

RESULTS: CDT levels were comparable between the two groups. GGT activities

were significantly greater in ALDH2(1)/2(1) than in ALDH2(1)/2(2) habitual drinkers (81 +/- 85 vs. 53 +/- 40 IU/liters, p < 0.02). MCV values, on the

other hand, were significantly larger in ALDH2(1)/2(2) than in ALDH2(1)/2(1) subjects (98.2 +/- 5.8 vs. 95.8 +/- 4.2 fl, p = 0.02). When we used elevation of either CDT or GGT to detect habitual drinking in ALDH2(1)/2(1) and 2(1)/2(2) subjects, the sensitivities were 57% and 46%, respectively. CDT levels were similar between habitual drinkers with normal aspartate aminotransferase levels and those with elevated levels. CONCLUSION: GGT and MCV, but not CDT, differ with respect to the ALDH2 genotypes in Japanese male habitual drinkers. ALDH2 genotypes should be considered when interpreting data on biological markers of **alcoholism**.

L138 ANSWER 2 OF 10 MEDLINE

DUPLICATE 2

96189048 Document Number: 96189048. **Nephelometric determination of carbohydrate deficient transferrin.** Schellenberg F; Martin M; Cac'es E; Benard J Y; Weill J. (Laboratory of Biochemistry, CHU Troussseau, Tours, France.) CLINICAL CHEMISTRY, (1996 Apr) 42 (4) 551-7. Journal code: DBZ. ISSN: 0009-9147. Pub. country: United States. Language: English.

AB We describe a technique for measuring **carbohydrate-deficient transferrin** (CDT) in serum. Serum transferrin fractions are separated by anion-exchange chromatography on microcolumns. Sialic acid-deficient transferrin fractions are collected in the eluate, and transferrin is then quantified by a **rate-nephelometric** Prepared by M. Hale 308-4258

technique. Imprecision (CV) was 4-5% within-run and 7-9% between runs (n = 15). Comparison with an isoelectric focusing-immunofixation method for **transferrin** index (x) yielded $y = 761x + 7$, $Sy/x = 39$ mg/L. Assay of sera from 90 abstainers or moderate consumers of alcohol showed that 81 (90%) had CDT concentrations between 30 and 70 mg/L. Among 74 alcoholics admitted to an alcohol treatment center, 54 (73%) had CDT > 70 mg/L, i.e., the diagnostic sensitivity was 73% at a specificity of 90% (area under receiver-operator characteristic curve = 0.891).

L138 ANSWER 3 OF 10 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
96291441 EMBASE Document No.: 1996291441. [AXIS% CDT RIA - A new marker of alcohol abuse]. AXIS% CDT RIA - NOVY TEST PRO PRUKAZ ABUZU ALKOHOLU.

Fingerova H.; Urbanek K.; Buresova J.. Porodnicka a Gynekologicka Klinika,

Lekarska Fakulta, Univerzita Palackeho, I.P. Pavlova 6,775 20 Olomouc, Czech Republic. Klinicka Biochemie a Metabolismus 4/3 (170-172) 1996. ISSN: 1210-7921. CODEN: KBMEFQ. Pub. Country: Czech Republic. Language: Czech. Summary Language: English; Czech.

AB Our first experience with a new test for simple and rapid detection of chronic high **alcohol consumption** in neurological patients is presented. The AXIS% CDT RIA kit uses an integrated **separation** and quantitation technique to measure the relative amount of **carbohydrate-deficient transferrin** (% CDT) in serum. So far, one hundred tests (two kits for 50 determinations) were performed on 70 serum samples from patients treated for neurological disorders and suspected of alcohol abuse during treatment, control individuals and out-patients with professional risk of liver damage. The preliminary evaluation and clinical interpretation give evidence of a significant reliability of the chosen analytical approach.

L138 ANSWER 4 OF 10 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
96289982 EMBASE Document No.: 1996289982. Reliability of **carbohydrate-deficient transferrin** to detect chronic alcohol misuse in carcinoma patients. Spies C.D.; Von Winterfeld A.; Muller C.; Rommelspacher H.; Neumann T.; Marks C.; Berger G.; Conrad C.; Blum S.; Hannemann L.; Striebel H.W.; Schaffartzik W.. Klin Anaesthesiol operat Intensivmed, Universitatsklinik Benjamin Franklin, Freie Universitat Berlin, Hindenburgdamm 30, D-12000 Berlin, Germany. European Addiction Research 2/3 (156-162) 1996.

ISSN: 1022-6877. CODEN: EADREE. Pub. Country: Switzerland. Language: English. Summary Language: English.

AB The patients' history and conventional laboratory markers are often not sensitive or specific enough to detect chronic alcohol misuse, preoperatively. We investigated whether **carbohydrate-deficient transferrin** (CDT), determined with a new commercially available kit, is a more sensitive and specific marker to detect chronic alcohol misuse in these patients and we compared it to a CDT research kit and to other conventional laboratory markers. 153 patients with oral, pharyngeal, laryngeal or esophageal carcinomas were evaluated regarding their **drinking** habits. Chronic **alcohol** misuse was diagnosed if the daily ethanol intake was ≥ 60 g and the patient met the DSM-III-R criteria for chronic alcohol abuse or dependence. CDTs and the conventional laboratory markers were sampled on admission of the patients, preoperatively, postoperatively

following admission to the ICU and on day 2, 4 and 7 in the ICU. CDT was determined by microanion exchange chromatography and turbidimetry (research kit) and microanion exchange chromatography and radioimmunoassay (commercially available CDT kit), respectively. The investigators were blinded to the CDT results. For all patients admitted to the hospital the sensitivity of the CDT research kit was 74% and for the commercially available CDT kit 77%. Specificity was 100% for the CDT research kit and 97% for the commercially available CDT kit. Both CDT kits were more accurate in detecting chronic alcohol misuse than any other conventional laboratory marker over a range of cutoffs evaluated

by receiver operating characteristic curves. Since the CDT values on admission were significantly correlated with the length of ICU stay (CDT research kit: $r(s) = 0.56$; $p = 0.000$; commercially available CDT: $r_s = 0.39$; $p = 0.009$) and since investigated chronic alcoholics developed more complications in the ICU and had a prolonged ICU stay, it seems reasonable to determine serum CDT, the most sensitive and specific marker of chronic alcohol misuse. Patients with pathologically elevated CDT values should be further evaluated and managed accordingly.

L138 ANSWER 5 OF 10 MEDLINE

DUPLICATE 3

97039828 Document Number: 97039828. Post mortem markers of chronic alcoholism. Sadler D W; Girela E; Pounder D J. (Department of Forensic Medicine, University of Dundee, Royal Infirmary, UK.) FORENSIC SCIENCE INTERNATIONAL, (1996 Sep 30) 82 (2) 153-63. Journal code: F49. ISSN: 0379-0738. Pub. country: Ireland. Language: English.

AB We compared the post mortem diagnostic value of gamma-glutamyltransferase (GGT), carbohydrate-deficient transferrin (CDT), alcoholic liver disease (ALD), blood alcohol concentration (BAC), the presence of multiple bruises and poor hygiene of the feet as markers of chronic alcoholism (heavy continuous drinking) in 32 alcoholics with 32 age-sex matched controls drawn from a forensic autopsy population. Alcoholics and controls were selected on the basis of positive and negative medical history but controls were excluded if BAC exceeded 70 mg%. Femoral venous blood, urine and vitreous humour alcohol concentrations were determined by headspace gas chromatography (GC). BAC was positive in 19 alcoholics (mean 234 mg%, range 2-570 mg%) and six controls (mean 32 mg%, range 2-52 mg%). Serum GGT was measured by a kinetic photometric method, and CDT by both isoelectric focusing/laser densitometry and by a commercial radioimmunoassay kit (CDTect). Features of alcoholic liver disease were graded histologically using two weighted scoring systems. Eleven alcoholics tested positive for GGT, CDTq and ALD, nine were positive for two tests, five for one test and three were negative for all three tests. No controls were positive for all three tests but six were positive for two tests and nine for only one test; 17 were negative for all three tests. Using the normal clinical cut-off values GGT, CDTq and CDTect gave poor specificity which was improved at moderate cost to sensitivity by raising cut off values for each test. Comparison of receiver operating characteristic curves, likelihood ratios and post-test odds showed CDT to be the best individual test, followed by ALD and GGT. Quantitation of CDT by IEF/laser densitometry performed slightly better than MAEC/RIA by CDTect. CDT shows considerable promise as a post mortem marker of chronic alcoholism.

L138 ANSWER 6 OF 10 MEDLINE

DUPLICATE 4

96042286 Document Number: 96042286. Relevance of **carbohydrate-deficient transferrin** as a predictor of alcoholism in intensive care patients following trauma. Spies C D; Emadi A; Neumann T; Hannemann L; Rieger A; Schaffartzik W; Rahmazadeh R; Berger G; Funk T; Blum S; et al. (Benjamin Franklin Medical Center, Department of Anesthesiology, Berlin, Germany.) JOURNAL OF TRAUMA, (1995 Oct) 39 (4) 742-8. Journal code: KAF. ISSN: 0022-5282. Pub. country: United States. Language: English.

AB Every second traumatized patient is a chronic alcoholic. Chronic alcoholics are at risk due to an increased morbidity and mortality. Reliable and precise diagnostic **methods** for detecting **alcoholism** are mandatory to prevent posttraumatic complications by adequate prophylaxis. The patient's history, however, is often not reliable, and conventional laboratory markers are not sensitive or specific enough. The aim of this study was to investigate whether **carbohydrate-deficient transferrin** (CDT) is a sensitive and specific marker to detect **alcoholism** in traumatized patients. One hundred and five male traumatized patients or their relatives gave their written informed consent to participate in this

institutionally approved study. All patients were transferred to the intensive care unit after admission to the emergency room, followed by surgical treatment. Diagnostics included an **alcoholism**-related questionnaire, conventional laboratory markers (mean corpuscular volume, gamma-glutamyltransferase, aspartate aminotransferase, and alanine aminotransferase), and CDT sampling (microanion-exchange chromatography, turbidimetry, and radioimmunoassay, respectively). Only patients in whom a reliable history could be obtained were included. **Alcoholism** was diagnosed if the patients met the Diagnostic and Statistical Manual of Mental Disorders criteria for chronic alcohol abuse or dependence. The administration of fluids before CDT sampling was carefully documented. Patients did not differ significantly regarding age,

Trauma and Injury Severity Score, and Acute Physiology and Chronic Health Evaluation score. The sensitivity of the CDT research **kit** was 70% and of the commercially available **kit** CDTect was 65%. Early sampling in the emergency room and before administration of large volumes of fluid increased the sensitivity to 83% for the CDT research **kit** and 74% for CDTect, respectively. (ABSTRACT TRUNCATED AT 250 WORDS)

L138 ANSWER 7 OF 10 MEDLINE

DUPLICATE 5

96099603 Document Number: 96099603. [Carbohydrate-deficient transferrin and liver diseases. Study of 94 patients]. Transferrine déficiente en acide sialique et maladies du foie. Etude de 94 malades. Ouyahya F; Bacq Y; Schellenberg F; Metman E H; Weill J. (Service d'Hepato-Gastroenterologie, Hopital Trousseau, Tours.) GASTROENTEROLOGIE CLINIQUE ET BIOLOGIQUE, (1995 Aug-Sep) 19 (8-9) 698-702. Journal code: FGX. ISSN: 0399-8320. Pub. country: France. Language: French.

AB OBJECTIVES AND METHODS--**Carbohydrate-deficient transferrin** has been proposed as a marker of alcohol consumption. The aim of this study was to evaluate the accuracy of the **carbohydrate-deficient transferrin** serum level, measured by ion exchange chromatography followed by radioimmunoassay (**Kit** CDTect), for the diagnosis of excessive

Prepared by M. Hale 308-4258

Page 28

alcohol intake in patients with liver diseases. Ninety-four patients (68 men, 26 women, age 21-71 years), 42 with alcoholic liver diseases and 52 with non-alcoholic liver diseases, were studied. Twenty-six patients consumed $> \text{ or } = 40$ g alcohol per day (mean alcohol intake: 84 ± 52 g per day) and were considered to be excessive drinkers. RESULTS--The sensitivity of **carbohydrate-deficient transferrin** for the diagnosis of excessive alcohol intake was 35%, and the specificity was 91%. By pairing **carbohydrate-deficient transferrin** with other markers of alcohol consumption, the sensitivity of the association of **carbohydrate-deficient transferrin** and gammaglutamyl transpeptidase was 96%, and the specificity was 59%. CONCLUSION--In patients with liver diseases, **carbohydrate-deficient transferrin** is a specific marker of excessive alcohol intake but a lack of sensitivity may limit its use.

L138 ANSWER 8 OF 10 MEDLINE DUPLICATE 6
95142434 Document Number: 95142434. [Multicenter study of sialic acid deficient **transferrin** determined by two chromatographic techniques]. Etude multicentrique du dosage de la **transferrine** déficiente en acide sialique par deux techniques chromatographiques. Vernet M; Renversez J C; Revenant M C; Sotta C; charlier De Bressing C; Benoit M O; Guillemin C; Paris M; Plomteux G. (Laboratoire de biochimie, hopital de la Croix-Rousse, Lyon, France.) ANNALES DE BIOLOGIE CLINIQUE, (1994) 52 (7-8) 535-46. Journal code: 4ZS. ISSN: 0003-3898. Pub. country: France. Language: French.

AB Serum **carbohydrate-deficient-transferrin** (CDT) was measured by a micro anion-exchange chromatography /enzyme immunoassay. Results obtained on 245 sera analyzed in four laboratories were compared. Moreover, one laboratory used a commercial kit with ready-to-use microcolumns and a radioimmunoassay for measuring eluted CDT. Imprecision was judged to be satisfactory. Within-assay coefficients of variation ranged from 5 to 10%, between-assay coefficients of variation ranged from 9 to 18%. Between-laboratory results were compared for 110 sera from control subjects (daily alcohol intake < 40 g), for 57 sera from chronic ethylic subjects and for 78 sera from patients suffering from non-alcoholic liver diseases. There was a large between-laboratory variation, suggesting that the **method** is difficult to standardize and that results are not transferable. Results of enzyme and radioimmunoassays were compared on 325 sera. The best correlation was obtained in the groups of ethylic subjects and those with non-alcoholic hepatic diseases. Finally the performance of the CDT-test was evaluated by calculating sensitivity and specificity. With both **methods** specificity was very high ($> 85\%$) but sensitivity was poor ($< 50\%$).

L138 ANSWER 9 OF 10 MEDLINE
94271349 Document Number: 94271349. Serum level of **carbohydrate-deficient transferrin** as a marker of alcoholic liver disease. Yamauchi M; Hirakawa J; Maezawa Y; Nishikawa F; Mizuhara Y; Ohata M; Nakajima H; Toda G. (First Department of Internal Medicine, Jikei Prepared by M. Hale 308-4258 Page 29

University School of Medicine, Tokyo, Japan.) ALCOHOL AND ALCOHOLISM.
SUPPLEMENT, (1993) 1B 3-8. Journal code: AAP. ISSN: 1358-6173. Pub.
country: ENGLAND: United Kingdom. Language: English.

AB Serum levels of **carbohydrate-deficient transferrin** (CDT) were assayed in 87 patients with alcoholic liver disease, 25 alcoholics without liver disease, 25 cases with viral liver disease and 37 healthy subjects, by two different **methods** (Pharmacia CDT RIA kit and Axis % CDT kit). The serum level of Pharmacia-CDT was significantly higher in the patients with alcoholic liver disease (38.9 +/- 2.8 U/l) compared to the normal subjects (18.9 +/- 0.2 U/l), alcoholics without liver disease (21.7 +/- 1.5 U/l) and non-alcoholic liver disease (viral liver disease) (23.4 +/- 1.6 U/l) (P < 0.001). The serum level of Axis-CDT was also significantly higher in the patients with alcoholic liver disease (4.22 +/- 0.48%) compared to the normal subjects (0.84 +/- 0.14%), alcoholics without liver disease (1.14 +/- 0.23%) and non-alcoholic liver disease (1.84 +/- 0.29%) (P < 0.001).

A significant correlation was found between serum levels of CDT determined by the two kits ($r = 0.718$, $P < 0.001$). The serum level of Axis-CDT was significantly higher in patients with alcoholic hepatitis compared to the normal subjects ($P < 0.005$), while the serum level of Pharmacia-CDT was not increased in the patients with alcoholic hepatitis. These results indicate that determination of serum CDT levels is a useful marker of alcoholic liver disease, not a marker for **alcohol consumption**. Axis-CDT is more useful than Pharmacia-CDT for assaying the serum level of CDT in patients with alcoholic liver disease.

L138 ANSWER 10 OF 10 MEDLINE DUPLICATE 7
93039033 Document Number: 93039033. Measurement of **carbohydrate-deficient transferrin** by isoelectric focusing/western blotting and by micro anion-exchange **chromatography** /radioimmunoassay: comparison of diagnostic accuracy. Xin Y; Rosman A S; Lasker J M; Lieber C S. (Alcohol Research & Treatment Center, Bronx Veterans Affairs Medical Center, NY.) ALCOHOL AND ALCOHOLISM, (1992 Jul) 27 (4) 425-33. Journal code: AAL. ISSN: 0735-0414. Pub. country:

ENGLAND:
United Kingdom. Language: English.

AB At present, the most reliable marker of recent and heavy alcohol intake is

carbohydrate-deficient transferrin (CDT).

While most CDT quantitation **methods** (including immunofixation and micro anion-exchange **chromatography** [MAEC] combined with radioimmunoassay [RIA]) either lack the precision required for diagnostic usage or are not commercially available, we recently described an isoelectric focusing/Western blotting (IEF/WB) procedure that provides sensitive and specific assessment of serum CDT content. However, a modified MAEC/RIA **kit**, supposedly more reliable than the original, is also being advanced as suitable for widespread clinical application. Therefore, we compared this modified MAEC/RIA procedure to the IEF/WB **method** of CDT quantitation in the following 108 subjects; 53 alcoholics undergoing detoxification without clinical or histological evidence of liver disease, 24 recently drinking alcoholics

Prepared by M. Hale 308-4258

Page 30

with biopsy-proven liver disease, eight alcoholics abstinent for more than 30 days with biopsy-proven liver disease, seven non-drinking patients with non-alcoholic liver disease, and 16 healthy controls. Although CDT measurements by the two **methods** were correlated ($r = 0.60$, $P < 0.01$), serum CDT values obtained with IEF/WB were nearly five-fold higher than those obtained with MAEC/RIA (e.g. 140.0 ± 58 versus 28.5 ± 16 mg/l among the active drinkers). Of the two **methods**, IEF/WB exhibited significantly greater sensitivity than MAEC/RIA for detecting recent, heavy drinking (75% versus 61%, $P < 0.05$) and generated no false positives whereas MAEC/RIA gave falsely elevated CDT levels in 37% of the abstinent alcoholics. (ABSTRACT. TRUNCATED AT 250 WORDS)

L139 20 FILE MEDLINE
L140 19 FILE CAPLUS
L141 9 FILE BIOSIS
L142 17 FILE EMBASE
L143 1 FILE WPIDS
L144 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L145 66 L109 AND ASSAY

=> s sundrehagen e?/au,in and l145

'IN' IS NOT A VALID FIELD CODE
L146 0 FILE MEDLINE
L147 0 FILE CAPLUS
L148 1 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L149 0 FILE EMBASE
L150 1 FILE WPIDS
L151 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L152 2 SUNDREHAGEN E?/AU,IN AND L145

=> dup rem l152

PROCESSING COMPLETED FOR L152
L153 2 DUP REM L152 (0 DUPLICATES REMOVED)

=> d 1-2 cbib abs

L153 ANSWER 1 OF 2 BIOSIS COPYRIGHT 2000 BIOSIS
1997:375425 Document No.: PREV199799674628. Semiautomated **carbohydrate**
-deficient transferrin for the diagnosis of alcohol
abuse. Bean, P. (1); Liegmann, K.; **Sundrehagen, E..** (1)
Specialty Lab., Santa Monica, CA USA. Alcoholism Clinical and
Experimental
Research, (1997) Vol. 21, No. 3, pp. 29A. Meeting Info.: Annual
Scientific

Prepared by M. Hale 308-4258

Page 31

Meeting of the Research Society on Alcoholism San Francisco, California,
USA July 19-24, 1997 ISSN: 0145-6008. Language: English.

L153 ANSWER 2 OF 2 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1996-402495 [40] WPIDS
AB WO 9626444 A UPAB: 19961007

Method for assessment of carbohydrate-deficient transferrin (CDTF) in a transferrin (TF) contg. **body fluid**, comprises:

(a) obtaining a TF contg. liq. sample of or derived from the fluid,
(b) contacting the sample with a source of iron ions,
(c) contacting the sample with an anionic ion exchange resin at a pH so as to cause CDTF to be retained by the resin,
(d) contacting the resin with an eluant to release the CDTF into the eluate,
(e) collecting a vol. of the eluate, free from tetra- and

penta-sialo TF and

(f) assessing the TF variant content in the vol. of eluate.

Also claimed are:

(1) a kit for a diagnostic **assay** for CDTF, comprising: (a') an iron ion contg. buffered incubation soln. having a pH of 6.2, (b') opt. a TF soln. of known concn., (c') an anionic ion exchange resin packed in a container having sample introduction and eluate removal ports,
(d') opt. a flushing eluant having a pH and ionic strength insufficient to release TF from the resin,
(e') a release eluant having a pH and ionic strength sufficient to release TF from the resin,

(f') opt. a light transmitting eluate receiving vessel,
(g') opt. an anti-TF antibody or fragment and

(h') opt. an opacification enhancer;
(2) a **method** for assaying for alcohol consumption, comprising assessing a **blood** derived **body**

fluid sample for its content of a de-sialo TF, characterised in that the de-sialo TF comprises tri-sialo TF and opt. 1 of di-sialo, mono-sialo and a sialo TF;

(3) a **method** for assaying for alcohol consumption, comprising:

(a'') obtaining a first TF contg. liq. sample of or derived form a **body fluid** and contg. tetra- and penta-sialo TFS,

(b'') obtaining from the first sample a second TF contg. liq. sample which is free form tetra- and penta-sialo TF and having a TF content of

1

mg/l and

(c'') turbidimetrically assessing the TF content of the second sample.

USE - The **method** is used for the **assay** of CDTF as an effective marker for alcohol consumption, in partic. for detecting and monitoring chronic alcohol consumption.

ADVANTAGE - Using the **method**, CDTF levels can be assessed using simple measurement techniques such as turbidimetry without needing signal amplification steps and while requiring only small **body fluid** samples.

Dwg.0/7

=> d 2

L153 ANSWER 2 OF 2 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1996-402495 [40] WPIDS
DNN N1996-339049 DNC C1996-126591
TI **Carbohydrate-deficient transferrin**
assay - using anionic ion exchange resin, used for assaying for
alcohol consumption.
DC B04 S03
IN SUNDREHAGEN, E
PA (AXIS-N) AXIS BIOCHEMICALS AS; (COCK-I) COCKBAIN J; (AXIS-N) AXIS-SHIELD
ASA
CYC 71
PI WO 9626444 A1 19960829 (199640)* EN 44p G01N033-68
RW: AT BE CH DE DK EA ES FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE
SZ UG
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS
JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT
RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN
AU 9647270 A 19960911 (199651) G01N033-68
NO 9703844 A 19971021 (199802) G01N033-68
EP 811166 A1 19971210 (199803) EN G01N033-68
R: AT BE CH DE DK ES FR GB GR IE IT LI NL SE
FI 9703432 A 19971017 (199804) G01N000-00
EP 854363 A1 19980722 (199833) EN G01N033-68
R: AT BE CH DE DK ES FR GB GR IE IT LI NL SE
US 5798212 A 19980825 (199841) G01N033-53
JP 11500227 W 19990106 (199911) 45p G01N033-68
AU 708780 B 19990812 (199944) G01N033-68
EP 811166 B1 19991006 (199946) EN G01N033-68
R: AT BE CH DE DK ES FR GB GR IE IT LI NL SE
DE 69604567 E 19991111 (199954) G01N033-68
ES 2140064 T3 20000216 (200016) G01N033-68
US 6103478 A 20000815 (200041) G01N033-53
ADT WO 9626444 A1 WO 1996-GB395 19960221; AU 9647270 A AU 1996-47270
19960221;
NO 9703844 A WO 1996-GB395 19960221, NO 1997-3844 19970821; EP 811166 A1
EP 1996-903125 19960221, WO 1996-GB395 19960221; FI 9703432 A WO
1996-GB395 19960221, FI 1997-3432 19970821; EP 854363 A1 Div ex EP
1996-903125 19960221, EP 1998-200650 19960221; US 5798212 A Cont of WO
1996-GB395 19960221, US 1996-716913 19960909; JP 11500227 W JP
1996-525494
19960221, WO 1996-GB395 19960221; AU 708780 B AU 1996-47270 19960221; EP
811166 B1 EP 1996-903125 19960221, WO 1996-GB395 19960221, Related to EP
1998-200650 19960221; DE 69604567 E DE 1996-604567 19960221, EP
1996-903125 19960221, WO 1996-GB395 19960221; ES 2140064 T3 EP
1996-903125
19960221; US 6103478 A CIP of WO 1996-GB395 19960221, Div ex US
1996-716913 19960909, US 1998-26156 19980219
FDT AU 9647270 A Based on WO 9626444; EP 811166 A1 Based on WO 9626444; EP
854363 A1 Div ex EP 811166; JP 11500227 W Based on WO 9626444; AU 708780
B
EP Previous Publ. AU 9647270, Based on WO 9626444; EP 811166 B1 Related to
EP

WO 854363, Based on WO 9626444; DE 69604567 E Based on EP 811166, Based on
9626444; ES 2140064 T3 Based on EP 811166; US 6103478 A Div ex US 5798212
PRAI GB 1995-16885 19950817; GB 1995-3484 19950222; GB 1995-6045
19950324
IC ICM G01N000-00; G01N033-53; G01N033-68
ICS G01N033-48; G01N033-543; G01N033-563; G01N033-98

=> dis his

(FILE 'HOME' ENTERED AT 10:23:45 ON 13 SEP 2000)
FILE 'REGISTRY' ENTERED AT 10:24:17 ON 13 SEP 2000
E TRANSFERRIN/CN 5
E CARBOHYDRATE FREE TRANSFERRIN/CN 5
L1 443 S ?TRANSFERRIN?/CNS
FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, WPIDS, JICST-EPLUS' ENTERED AT
10:25:24 ON 13 SEP 2000
L2 411 FILE MEDLINE
L3 208 FILE CAPLUS
L4 331 FILE BIOSIS
L5 427 FILE EMBASE
L6 15 FILE WPIDS
L7 4 FILE JICST-EPLUS
TOTAL FOR ALL FILES
L8 1396 S (L1 OR ?TRANSFERRIN? OR SIDEROPHILIN? OR
(D12.775.124.50.800
L9 0 FILE MEDLINE
L10 2 FILE CAPLUS
L11 0 FILE BIOSIS
L12 0 FILE EMBASE
L13 2 FILE WPIDS
L14 0 FILE JICST-EPLUS
TOTAL FOR ALL FILES
L15 4 S L8(10A)CARBOHYDRATE FREE
L16 2 DUP REM L15 (2 DUPLICATES REMOVED)
L17 260 FILE MEDLINE
L18 145 FILE CAPLUS
L19 245 FILE BIOSIS
L20 251 FILE EMBASE
L21 6 FILE WPIDS
L22 1 FILE JICST-EPLUS
TOTAL FOR ALL FILES
L23 908 S L8(10A)CARBOHYDRATE DEFICIEN?
L24 376 FILE MEDLINE
L25 236 FILE CAPLUS
L26 459 FILE BIOSIS
L27 382 FILE EMBASE
L28 8 FILE WPIDS
L29 25 FILE JICST-EPLUS
TOTAL FOR ALL FILES
L30 1486 S (CARBOHYDRATE(W) (FREE OR DEFICIEN?)) (5A) (L1 OR
?TRANSFERRIN?)

Prepared by M. Hale 308-4258

Page 34

L31 260 FILE MEDLINE
L32 145 FILE CAPLUS
L33 245 FILE BIOSIS
L34 251 FILE EMBASE
L35 3 FILE WPIDS
L36 1 FILE JICST-EPLUS
TOTAL FOR ALL FILES
L37 905 S L30(10A) (ALCOHOLISM OR ALCOHOL(2A) (CONSUMP? OR DRINK?) OR
TEM
L38 8 FILE MEDLINE
L39 14 FILE CAPLUS
L40 7 FILE BIOSIS
L41 6 FILE EMBASE
L42 0 FILE WPIDS
L43 0 FILE JICST-EPLUS
TOTAL FOR ALL FILES
L44 35 S L37 AND (ASIALO OR MONOSIALO OR TRISIALO OR TETRASIALO OR
PEN
L45 8 FILE MEDLINE
L46 13 FILE CAPLUS
L47 7 FILE BIOSIS
L48 6 FILE EMBASE
L49 0 FILE WPIDS
L50 0 FILE JICST-EPLUS
TOTAL FOR ALL FILES
L51 34 S L44 NOT L15
L52 15 DUP REM L51 (19 DUPLICATES REMOVED)
L53 252 FILE MEDLINE
L54 131 FILE CAPLUS
L55 238 FILE BIOSIS
L56 245 FILE EMBASE
L57 3 FILE WPIDS
L58 1 FILE JICST-EPLUS
TOTAL FOR ALL FILES
L59 870 S L37 NOT L44
L60 252 FILE MEDLINE
L61 130 FILE CAPLUS
L62 238 FILE BIOSIS
L63 245 FILE EMBASE
L64 1 FILE WPIDS
L65 1 FILE JICST-EPLUS
TOTAL FOR ALL FILES
L66 867 S L59 NOT L15
L67 4 FILE MEDLINE
L68 2 FILE CAPLUS
L69 2 FILE BIOSIS
L70 1 FILE EMBASE
L71 0 FILE WPIDS
L72 0 FILE JICST-EPLUS
TOTAL FOR ALL FILES
L73 9 S L66 AND (BIND? LIGAND OR LECTIN?)
L74 6 DUP REM L73 (3 DUPLICATES REMOVED)
L75 248 FILE MEDLINE
L76 128 FILE CAPLUS
L77 236 FILE BIOSIS
L78 244 FILE EMBASE

L79 1 FILE WPIDS
L80 1 FILE JICST-EPLUS
TOTAL FOR ALL FILES
L81 858 S L66 NOT L73
L82 0 FILE MEDLINE
L83 0 FILE CAPLUS
L84 0 FILE BIOSIS
L85 0 FILE EMBASE
L86 0 FILE WPIDS
L87 0 FILE JICST-EPLUS
TOTAL FOR ALL FILES
L88 0 S (SAMBUCK? OR MAACK? OR ESCHERCHIA OR HELICOBACTER OR RICIN?
OR
L89 224 FILE MEDLINE
L90 79 FILE CAPLUS
L91 87 FILE BIOSIS
L92 132 FILE EMBASE
L93 1 FILE WPIDS
L94 1 FILE JICST-EPLUS
TOTAL FOR ALL FILES
L95 524 S L81 AND BLOOD
L96 0 FILE MEDLINE
L97 2 FILE CAPLUS
L98 1 FILE BIOSIS
L99 0 FILE EMBASE
L100 1 FILE WPIDS
L101 0 FILE JICST-EPLUS
TOTAL FOR ALL FILES
L102 4 S L81 AND BODY FLUID
L103 109 FILE MEDLINE
L104 49 FILE CAPLUS
L105 57 FILE BIOSIS
L106 68 FILE EMBASE
L107 1 FILE WPIDS
L108 0 FILE JICST-EPLUS
TOTAL FOR ALL FILES
L109 284 S (L95 OR L102) AND (DETERM? OR DETM OR METHOD)
L110 31 FILE MEDLINE
L111 18 FILE CAPLUS
L112 14 FILE BIOSIS
L113 19 FILE EMBASE
L114 0 FILE WPIDS
L115 0 FILE JICST-EPLUS
TOTAL FOR ALL FILES
L116 82 S L109 AND (SEPARAT? OR PRECIPIT? OR CENTRIFUG? OR FILT? OR
CHR
L117 1 FILE MEDLINE
L118 1 FILE CAPLUS
L119 0 FILE BIOSIS
L120 1 FILE EMBASE
L121 0 FILE WPIDS
L122 0 FILE JICST-EPLUS
TOTAL FOR ALL FILES
L123 3 S L116 AND (TURBIDOMET? OR NEPHELOMET?)
L124 7 FILE MEDLINE
L125 2 FILE CAPLUS

Prepared by M. Hale 308-4258

Page 36

L126 5 FILE BIOSIS
L127 5 FILE EMBASE
L128 0 FILE WPIDS
L129 0 FILE JICST-EPLUS
TOTAL FOR ALL FILES
L130 19 S L116 AND KIT
L131 8 FILE MEDLINE
L132 3 FILE CAPLUS
L133 5 FILE BIOSIS
L134 6 FILE EMBASE
L135 0 FILE WPIDS
L136 0 FILE JICST-EPLUS
TOTAL FOR ALL FILES
L137 22 S L123 OR L130
L138 10 DUP REM L137 (12 DUPLICATES REMOVED)
L139 20 FILE MEDLINE
L140 19 FILE CAPLUS
L141 9 FILE BIOSIS
L142 17 FILE EMBASE
L143 1 FILE WPIDS
L144 0 FILE JICST-EPLUS
TOTAL FOR ALL FILES
L145 66 S L109 AND ASSAY
L146 0 FILE MEDLINE
L147 0 FILE CAPLUS
L148 1 FILE BIOSIS
L149 0 FILE EMBASE
L150 1 FILE WPIDS
L151 0 FILE JICST-EPLUS
TOTAL FOR ALL FILES
L152 2 S SUNDREHAGEN E?/AU, IN AND L145
L153 2 DUP REM L152 (0 DUPLICATES REMOVED)

=> s l145 not (l152 or l130 or l123 or l73 or l44 or l15)

L154 17 FILE MEDLINE
L155 17 FILE CAPLUS
L156 6 FILE BIOSIS
L157 16 FILE EMBASE
L158 0 FILE WPIDS
L159 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L160 56 L145 NOT (L152 OR L130 OR L123 OR L73 OR L44 OR L15)

=> dup rem l160

PROCESSING COMPLETED FOR L160
L161 32 DUP REM L160 (24 DUPLICATES REMOVED)

=> d cbib abs 1-32

L161 ANSWER 1 OF 32 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
2000198926 EMBASE [Carbohydrate deficient
transferrin, the use as marker for alcohol abuse].
Prepared by M. Hale 308-4258

KOOLHYDRAATDEFICIENT TRANSFERRINE: BETEKENIS ALS MARKER VOOR ALCOHOLMISBRUIK. Kreutzer H.J.H.; Van Pelt J.. Dr. H.J.H. Kreutzer, Vinkelstraat 163, 5382 JA Vinkel, Netherlands. Nederlands Tijdschrift voor de Klinische Chemie 25/3 (166-169) 2000.

Refs: 31.

ISSN: 1380-3689. CODEN: NTKCFX. Pub. Country: Netherlands. Language: Dutch. Summary Language: English; Dutch.

AB There is a urgent need for tests that can detect chronic alcohol abuse. Several studies are published on the influence of high ethanol intake on the reduced glycosylation of **transferrin**, resulting in **carbohydrate-deficient transferrin**.
Methods for the separation of **carbohydrate-deficient transferrin** involve either iso-electric focussing or ion exchange chromatography. The latter principle is used for routine assays with automated equipment for the **transferrin determination**. Possibly, the percentage of the deficient isoforms to the total **transferrin** amount is less susceptible to variations in the total **transferrin** concentration as the absolute concentration of **carbohydrate-deficient transferrin**. The CDT test, in combination with the GGT, has a very high specificity and the sensitivity is acceptable merely when the test is used for patients with serious suspicion of alcohol abuse. In other cases, up to 50% false negatives can be detected.

L161 ANSWER 2 OF 32 MEDLINE

2000203534 Document Number: 20203534. Stability of **carbohydrate-deficient transferrin** (CDT) in stored **blood** samples. Kohler H; West A; Brinkmann B. (Institute of Legal Medicine, Westfälische Wilhelms-Universität, Münster, Germany.. kohlerh@uni-muenster.de) . INTERNATIONAL JOURNAL OF LEGAL MEDICINE, (2000) 113 (2) 121-2. Journal code: AX1. ISSN: 0937-9827. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB The **alcoholism** marker CDT was **determined** on 257 **blood** samples 1-2 days after the **blood** samples were taken and again after storage for 7 months at +4 degrees C. The differences between the pairs of CDT values were so large that the **determination** of CDT after long term storage of the **blood** sample has no evidential value.

L161 ANSWER 3 OF 32 MEDLINE

DUPPLICATE 1

2000016185 Document Number: 20016185. Relative versus absolute **carbohydrate-deficient transferrin** as a marker of alcohol consumption in patients with acute alcoholic hepatitis. Halm U; Tannapfel A; Mossner J; Berr F. (Department of Medicine II, University of Leipzig, Germany.. halmu@medizin.uni-leipzig.de) . ALCOHOLISM, CLINICAL AND EXPERIMENTAL RESEARCH, (1999 Oct) 23 (10) 1614-8. Journal code: 35X. ISSN: 0145-6008. Pub. country: United States. Language: English.

AB BACKGROUND: **Carbohydrate-deficient transferrin** has been described as a sensitive and specific marker for **alcohol consumption**. This study investigated the usefulness of **carbohydrate-deficient transferrin** as a marker of alcohol consumption in acute alcoholic hepatitis.

METHODS: Absolute concentrations (U/I) and relative values (%) of Prepared by M. Hale 308-4258 Page 38

carbohydrate-deficient transferrin
determined in serum with commercial assays, as well as conventional markers for alcohol consumption, were compared with the alcohol consumption (as estimated by a questionnaire) in patients with acute alcoholic hepatitis (n = 19), alcoholic liver cirrhosis (n = 37), and nonalcoholic liver diseases (n = 16). RESULTS: The concentration of **carbohydrate-deficient transferrin** was increased ($p < 0.001$) in nonabstaining patients (median intake 80 g alcohol/day) with alcoholic liver cirrhosis (45.7 \pm 30 U/l), but not in patients with acute alcoholic hepatitis (20.0 \pm 7.8 U/l) despite higher **alcohol consumption** (median 130 g/d), nor in abstainers with alcoholic liver cirrhosis (19.4 \pm 6.0 U/l) or nonalcoholic liver disease (18.5

+/-

6.7 U/l). However, the relative values of **carbohydrate-deficient transferrin** were increased both in acute alcoholic hepatitis (7.9 \pm 2.1%) and nonabstainers with alcoholic liver cirrhosis (7.4 \pm 2.8%), but not in abstainers with alcoholic liver cirrhosis (4.6 \pm 3.5%) or nonalcoholic liver disease (3.8 \pm 0.9%) (p

<

0.001). In acute alcoholic hepatitis, the sensitivity and specificity were

only 32% and 87% for absolute concentrations, respectively, but 79% and 97% for relative values of **carbohydrate-deficient transferrin**. The concentrations of **carbohydrate-deficient** and total **transferrin** in serum were strongly correlated ($r = 0.60$; $p = 0.008$). CONCLUSIONS: The relative value (% of total), but not the absolute concentration, of **carbohydrate-deficient transferrin** in serum is a useful marker of **alcohol consumption** in acute alcoholic hepatitis.

L161 ANSWER 4 OF 32 MEDLINE

1999323417 Document Number: 99323417. Sialic acid: new potential marker of alcohol abuse. Sillanaukee P; Ponnio M; Seppa K. (Pharmacia & Upjohn AB Diagnostics, Alcohol Related Diseases, Uppsala, Sweden..

pekka.sillanaukee@sci.fi) . ALCOHOLISM, CLINICAL AND EXPERIMENTAL

RESEARCH,

(1999 Jun) 23 (6) 1039-43. Journal code: 35X. ISSN: 0145-6008. Pub. country: United States. Language: English.

AB BACKGROUND: A number of laboratory markers are suggested for the detection

and monitoring of alcohol abuse. However, there is still a need to find better indicators of alcohol abuse. Sialic acid (SA) is the name for a series of acyl-derivatives of neuraminic acids that occur as nonreducing terminal residues of glycoproteins or glycolipids in biological fluids

and

cell membranes. In this study, we investigated the diagnostic value of SA as a marker of alcohol abuse. METHODS: Sera from social drinkers (n = 38) and alcoholics (n = 77) were analyzed for sialic acid by a colorimetric assay and for **carbohydrate-deficient transferrin** (CDT) by a radioimmunoassay method. Mean corpuscular volume (MCV), gamma-glutamyltransferase (GGT), aspartate aminotransferase (ASAT), and alanine aminotransferase (ALAT) were determined by using routine methods.

RESULTS: The sialic acid levels of both female and male subjects were significantly ($p < 0.001$) increased among alcoholic subjects when compared

with social drinkers. SA levels were decreased after 3 weeks of treatment.

The sensitivity and specificity for SA, respectively, were 57.7 and 95.5 for women and 47.8 and 81.3 for men. The respective values for CDT were 57.7 and 95.5 for women and 78.3 and 100.0 for men; for GGT, 60.0 and 95.5 for women and 60.9 and 87.5 for men; for MCV, 52.4 and 95.5 for women and 47.8 and 100.0 for men; for ASAT, 53.8 and 95.5 for women and 43.5 and 100.0 for men; and for ALAT, 38.5 and 90.9 for women and 39.1 and 87.5 for

men. Among women, SA and GGT, and among men CDT, showed the largest area under receiver operation curve. CONCLUSION: This study indicated that sialic acid levels were elevated by high alcohol consumption and reduced during abstinence, especially among women. Thus, sialic acid seems to be an interesting marker that needs further evaluation as a diagnostic tool for alcohol abuse.

L161 ANSWER 5 OF 32 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 2
1999:646163 Document No. 131:282645 Evaluation of the cut-off for serum **carbohydrate-deficient transferrin** as a marker of chronic alcohol abuse determined by the ChronAlco I.D. TM-assay. Arndt, Torsten; Behnken, L. J.; Martens, B.; Hackel, R. (Institut Laboruntersuchungen Ingelheim G.m.b.H., Ingelheim, D-55218, Germany). Laboratoriumsmedizin, 23(9), 507-510 (English) 1999. CODEN: LABOD3. ISSN: 0342-3026. Publisher: Blackwell Wissenschafts-Verlag GmbH.

AB The aim of the study was to establish reliable cut-off values, indicating chronic alc. abuse, of the relative (and abs.) serum **carbohydrate-deficient transferrin** (CDT) concns. detd. by the ChronAlco I.D.-assay. Serum samples from 88 women and 48 men, with the daily alc. consumption, acute or chronic (liver) diseases and medication ascertained by means of a questionnaire, were analyzed. The cut-off values of the CDT/transferrin ratios and the CDT serum concns. (95th percentiles) for women consuming < 20 g ethanol/day and men drinking < 50 g ethanol/day were 2.5% and 102 mg/L. Pathol. CDT results were confirmed by isoelec. focusing. Taking into account the intra-individual variance of serum CDT and the anal. imprecision, the use of a borderline of 2.5-2.7% as decision criterion indicating chronic alc. abuse is suggested.

L161 ANSWER 6 OF 32 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 3
1999:482396 Document No. 131:127336 Relative and absolute CDT concentrations in sera from anemic patients measured by commercial immunoassays following miniaturized column chromatography and by high performance liquid chromatography. Niemeier, Anja; Blocker, Kathrin; Dibbelt, Leif (Inst. Klinische Chem., Med. Univ. Lubeck, Lubeck, D-23538, Germany). Clin. Lab. (Heidelberg), 45(7/8), 371-376 (English) 1999. CODEN: CLLAfp.

Publisher:

Clin Lab Publications.

AB Detn. of **carbohydrate-deficient transferrin** (CDT) is frequently used as a lab. tool for the diagnosis and follow-up of chronically increased alc. consumption. To study the effect of iron deficiency anemia on CDT

Prepared by M. Hale 308-4258

Page 40

concs., 200 sera from patients presenting with decreased Hb and ferritin levels were analyzed for relative CDT concn. using the new Tina-quant %CDT immunoturbidimetric assay on a Hitachi 717 analyzer (Roche Diagnostics). The results were compared to abs. CDT concns. obtained with an established CDT RIA (CDTect, Pharmacia & Upjohn) and to relative CDT concns. detd. by high performance liq. chromatog. (HPLC) in the same sera. The data measured with the three methods show only a weak correlation (correlation coeffs. < 0.5), apparently not only due to a difference between abs. and relative CDT concns. but also to the fact that different patterns of hyposialylated isotransferrins are detected by the various assays. No sample exhibited increased CDT concn. when assayed by HPLC indicating that iron deficiency anemia does not cause marked changes in transferrin glycan compn. When the abs. CDT concn. was measured by the CDTect RIA it was slightly to markedly increased in 54 of the 200 sera tested. The Tina-quant %CDT assay, however, yielded relative CDT concns. above the decision limit for chronically increased alc. consumption in only 5 sera.

L161 ANSWER 7 OF 32 BIOSIS COPYRIGHT 2000 BIOSIS
2000:54456 Document No.: PREV200000054456. Limitations of CDT and GGT in detecting relapses in patients attending an alcohol problems clinic. Limin, S.; Jarvie, D. R.; Chick, J. (1); Simpson, D. (1) Alcohol Problems Clinic, 35 Morningside Park, Edinburgh, EH10 5HD UK. Scottish Medical Journal, (Oct., 1999) Vol. 44, No. 5, pp. 140-142. ISSN: 0036-9330. Language: English. Summary Language: English.

AB Biochemical markers of alcohol consumption are useful for the detection and monitoring of problem drinking. Blood samples from 37 patients attending an alcohol treatment clinic were analysed for GGT and %CDT, and results were compared with self-reported periods of abstinence and alcohol consumption. Poor correlation was obtained between GGT and %CDT, and between these assays and self-reported alcohol use. The apparent sensitivity and specificity of GGT (57%, 63%) and %CDT (43%, 88%), were considerably lower than those reported by other workers.

L161 ANSWER 8 OF 32 MEDLINE DUPLICATE 4
1999113048 Document Number: 99113048. Absolute or relative measurement of carbohydrate-deficient transferrin in serum? Experiences with three immunological assays. Helander A. (Karolinska Institutet, Departments of Clinical Neuroscience and Clinical Chemistry, Alcohol and Drug Dependence Unit at Karolinska Hospital, SE-17176 Stockholm, Sweden.. anders.helander@bek1.css1.sll.se) . CLINICAL CHEMISTRY, (1999 Jan) 45 (1) 131-5. Journal code: DBZ. ISSN: 0009-9147. Pub. country: United States. Language: English.

L161 ANSWER 9 OF 32 MEDLINE DUPLICATE 5
1998432388 Document Number: 98432388. Intra- and interindividual variability of carbohydrate-deficient transferrin. Prepared by M. Hale 308-4258

gamma-glutamyltransferase, and mean corpuscular volume in teetotalers.
Helander A; Vabo E; Levin K; Borg S. (Department of Clinical Neuroscience,
Karolinska Institute, Center for Dependency Disorders at St. Gorans & Karolinska Hospital, Stockholm, Sweden.. anders.helander@bekl.css.sll.se)
. CLINICAL CHEMISTRY, (1998 Oct) 44 (10) 2120-5. Journal code: DBZ.
ISSN: 0009-9147. Pub. country: United States. Language: English.
AB Blood samples for determination of the biochemical alcohol markers **carbohydrate-deficient transferrin** (CDT) in serum, gamma-glutamyltransferase (GGT) in serum, and erythrocyte mean corpuscular volume (MCV) were collected once every 1-2 weeks over approximately 5 months from 10 female and 4 male teetotalers. Mean values for serum CDT (using the CDTect assay) ranged from 9.9 to 29.4 units/L (median, 14.2 units/L), and the highest results were obtained in the women. The mean values for serum GGT ranged from 0.15 to 0.49 microkat/L (median, 0.30 microkat/L, or 18 U/L) except for one woman with a very high mean of 3.07 microkat/L. For MCV, the mean values ranged from 79.5 to 91.5 fL. Two women showed several CDT results above the upper reference limit (mean values, 27.6 and 29.4 units/L, respectively); however, their GGT and MCV values fell within the reference intervals. One of these women exhibited an increased total **transferrin** concentration (mean value, 5.38 g/L), which was possibly related to the use of oral contraceptives and/or a low serum iron concentration. When the CDTect value was expressed relative to total **transferrin**, a ratio within the reference interval was observed for this woman but not for the other woman with increased CDTect values. The present study demonstrates a considerable variation between individuals in CDT, GGT, and MCV without **drinking any alcohol**. The results also show that these baseline values are fairly constant over time within the same individual.

L161 ANSWER 10 OF 32 MEDLINE
1999050964 Document Number: 99050964. **Carbohydrate-deficient transferrin: diagnostic efficiency among patients with end-stage liver disease before and after liver transplantation.** Heinemann A; Sterneck M; Kuhlencordt R; Rogiers X; Schulz K H; Queen B; Wischhusen F; Puschel K. (Institute of Legal Medicine, University Hospital Hamburg, Germany.) ALCOHOLISM, CLINICAL AND EXPERIMENTAL RESEARCH, (1998 Nov) 22 (8) 1806-12. Journal code: 35X.
ISSN: 0145-6008. Pub. country: United States. Language: English.
AB We tested the diagnostic validity of **carbohydrate-deficient transferrin** (CDT) as an indicator for relapse into elevated **alcohol consumption** among patients who were examined under follow-up treatment before (n = 147) and after (n = 102) orthotopic liver transplantation (OLT) in the outpatient-department of the University Hospital Department of Surgery in Hamburg-Eppendorf.
CDT measurements were performed with two commercial kits in parallel (CDTect-RIA and CDT%-RIA). Short-term parameters of **alcohol consumption** (ethanol, methanol) indicated relapses into elevated **alcohol consumption** in 11.4% of the evaluated patients
Prepared by M. Hale 308-4258

with alcoholic liver disease (ALD) before transplantation. Before OLT, median CDT values were determined to be elevated among patients with alcoholic as well as nonalcoholic end-stage liver diseases (NALD). Among patients with ALD, we found elevated CDT medians even in those who were successfully scheduled for OLT after long-term evidence of abstinence

proved by biochemical short-term parameters and psychological tests. Both CDTect and CDT% assays had comparable low specificities in selected patient groups before transplantation. CDT% and CDTect were negatively correlated with the albumin level. Before the study ended, CDT was no longer implemented in the evaluation of whether an OLT should be administered. This was due to inconsistent results of CDT in ALD as well as NALD. After OLT, patients with ALD, as well as NALD, had statistically significant lower CDT medians than before OLT, which ranged within reference levels. We determined, according to CDT, elevated alcohol consumption subsequent to OLT in 4 of 13 patients with ALD who underwent transplantation during the study (median observation period: 10 months). CDT does not appear to be useful in evaluating patients before OLT. With regained specificity and high sensitivity in patients after OLT, CDT could be recommended as a standard instrument for quality control in patients with ALD after liver transplantation.

L161 ANSWER 11 OF 32 MEDLINE

DUPLICATE 6

1998286708 Document Number: 98286708. Comparison of the Axis %CDT TIA and the CDTect method as laboratory tests of alcohol abuse. Viitala K; Lahdesmaki K; Niemela O. (EP Central Hospital Laboratory, Seinajoki, Finland.) CLINICAL CHEMISTRY, (1998 Jun) 44 (6 Pt 1) 1209-15. Journal code: DBZ. ISSN: 0009-9147. Pub. country: United States. Language: English.

AB Carbohydrate-deficient transferrin (CDT) has been suggested as a specific marker of alcohol abuse. We designed this study to compare the conventional CDTect method (Pharmacia & Upjohn) and the new semiautomated Axis %CDT turbidimetric immunoassay (%CDT TIA) for their diagnostic performance to identify problem drinking. The sensitivities of the %CDT TIA and CDTect for correctly classifying heavy drinkers ($n = 90$) were 29% and 59% with the thresholds currently recommended by the manufacturers, respectively. In the control group ($n = 114$), which included hospitalized patients with abnormal serum transferrin concentrations, the CDTect assay gave 21 false-positive values (18%), whereas the %CDT TIA showed 100% specificity.

With the cutoff limits based on the present healthy control group (mean + 2 SD), the sensitivities of the %CDT TIA and CDTect were 61% and 86%, respectively. For men, the ROC plot area of the CDTect results in comparisons of alcohol abusers and healthy controls was significantly ($P <$

0.05) higher than that of the %CDT TIA results, whereas for women, there was no significant difference in this respect. The slope and intercept (with 95% confidence intervals) for linear regression between CDTect and %CDT TIA were 0.13 (0.12-0.15) and 1.16 (0.73-1.59), respectively ($S(y/x) = 1.51$, $r = 0.744$). CDTect results correlated positively with serum transferrin ($r = 0.224$, $P < 0.001$), whereas the %CDT TIA results showed a slight inverse correlation with serum transferrin ($r = -0.132$, $P = 0.07$). The data suggest that CDTect is more sensitive than %CDT TIA in detecting drinking problems. However, the %CDT TIA

Prepared by M. Hale 308-4258

Page 43

method yields more specificity when analyzing samples from patients with high serum **transferrin** concentrations.

L161 ANSWER 12 OF 32 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 7
1998:341157 Document No. 129:119850 **Carbohydrate deficient transferrin** in alcoholic and non-alcoholic liver disease: a comparison of two **assay methods**. Keating, James; Cheung, Connie; Peters, Timothy J.; Przemioslo, Robert; Williams, Roger; Sherwood, Roy A. (Department of Clinical Biochemistry, King's College School of Medicine and Dentistry, London, SE5 9PJ, UK). *Addict. Biol.*, 3(2), 205-211 (English) 1998. CODEN: ADBIFN. ISSN: 1355-6215. Publisher: Carfax Publishing Ltd..

AB **Carbohydrate-deficient transferrin** (CDT) was assayed in 105 patients with non-alc.-related liver diseases, 50 patients with alc.-induced liver disease and 40 alc. abusers with minimal hepatic dysfunction. The patients with liver disease were hospitalized for assessment of suitability for orthotopic liver transplantation. CDT was measured by two com. available micro anion exchange **methods**; CDTect (Pharmacia) and %CDT (AXIS). Addnl., total **transferrin** was measured to allow expression of the CDTect results as "relative" measurements. Overall, 41/105 (39%) of patients with non-alc.-related liver diseases had a raised CDTect result, 13/105 (12%) had a raised %CDT result and 26/105 (25%) an abnormal CDTect/total **transferrin** ratio. In general, patients with cholestatic liver disease, primary biliary cirrhosis or primary sclerosing cholangitis had more "false pos." results by CDTect than did those with viral or autoimmune hepatitis. The sensitivity of the two **methods** for the detection of alc. misuse was similar; CDTect 77%, %CDT 65% and CDTect/total **transferrin** ratio 70%. This was, however, lower than the sensitivity of the conventional marker GGT (82%). In patients with severe liver disease, where up to 30% of the serum total **transferrin** concns. fall outside the ref. range, "relative" CDT **methods** have greater specificity than "abs." measurements.

L161 ANSWER 13 OF 32 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 8
1998:323516 Document No. 128:318276 Examination of biochemical **alcoholism** parameters in **blood** samples of drivers under the influence of alcohol; with particular reference to **carbohydrate deficient transferrin**. Heinemann, Axel; Janke, Detlef; Pueschel, Klaus (Inst. Rechtsmedizin, Krankenhaus Eppendorf, Hamburg, D-22529, Germany). *Blutalkohol*, 35(3), 161-173 (German) 1998. CODEN: BLALAL. ISSN: 0006-5250. Publisher: Steintor-Verlag.

AB Blood samples of drunk driving offenders were exmd. for sensitivity of current proceedings. Threshold values of **blood** alc. concn. (BAC, 1.6 or 2.0 .permill.) were analyzed by biochem. **alcoholism** parameters. MeOH, **carbohydrate deficient transferrin** (CDT%), and .gamma.-glutamyl transferase (GGT) were analyzed (group A: 1.1-1.59; B: 1.6-1.99; and C: >2.0 .permill.). Relevant groups of people in all 3 BAC categories fell within the normal range for markers of **alcoholism**. 24% In group B were inconspicuous, 68% in group A showed at least 1 elevation in parameter. The study emphasized a certain arbitrariness when choosing BAC indicator limits above 1.1 .permill.. Similar results to the ones achieved by CDT% **assay** were found using other **methods**
Prepared by M. Hale 308-4258

of CDT detn. Unlike to GGT, CDT% showed no dependency on age. An increasing no. of problematic values of GGT and CDT% was found in samples taken in the afternoon. For certain BAC areas no correlation was found between relative drinking symptomatics and GGT/CDT% measurements. The results were discussed with relevance to the altered legislation outline to exclude future scientific studies of similar concept.

L161 ANSWER 14 OF 32 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 9
1997:759931 Document No. 128:19448 Determination of carbohydrate-deficient transferrin and total transferrin by HPLC. Diagnostic evaluation. Renner, Florian; Stratmann, Karen; Kanitz, Rolf Dieter; Wetterling, Tilman (Inst. Klinische Chemie, Medizinische Univ. Luebeck, Luebeck, Germany). Clin. Lab. (Heidelberg), 43(11), 955-964 (English) 1997. CODEN: CLLAfp. Publisher: Clin Lab Publications.

AB The HPLC for detn. of carbohydrate-deficient transferrin (CDT) was compared with respect to its diagnostic validity with a com. assay (CDTect). Samples from alc. abusers characterized by alc. dependence and alc. withdrawal syndrome with elevated .gamma.-glutamyltransferase and mean corpuscular vol. of erythrocytes were analyzed by different methods. For males correlation between all methods was satisfactory, whereas for females the correlation between RIA and HPLC was low. Cut-off levels of 2.4% and 75 mg/L for relative and abs. HPLC measurements were calcd. The highest values for sensitivity, neg. predictive values and areas under

ROC curves were obtained when the relative CDT values were detd. by HPLC. The method was suitable for simultaneous detn. of total transferrin concn.

L161 ANSWER 15 OF 32 CAPLUS COPYRIGHT 2000 ACS
1997:560000 Document No. 127:231514 Comparison of two commercial test kits for quantification of serum carbohydrate-deficient transferrin. Stowell, L. I.; Fawcett, J. P.; Brooke, M.; Robinson, G. M.; Stanton, W. R. (Institute of Environmental Science and Research Ltd (ESR), Lower Hutt, N. Z.). Alcohol Alcohol. (Oxford), 32(4), 507-516 (English) 1997. CODEN: ALALDD. ISSN: 0735-0414. Publisher: Oxford University Press.

AB Serum levels of carbohydrate-deficient transferrin (CDT) were measured in subjects of two independent studies using two different com. kits. The kits measure CDT either as a percentage of total transferrin (AXIS %CDT, AXIS Biochems. AS, Norway), or as the abs. amt. (CDTect, Pharmacia, Sweden). In a population

of males (mean age 41 yr) consisting of alcoholics, heavy, moderate and non-drinkers, a strong correlation was found between AXIS %CDT and CDTect results ($r = 0.92$, $n = 58$, $P < 0.001$). Sensitivity and specificity in detecting chronic alc. drinking of over 60 g/day were 78 and 94% for the AXIS assay, and 83 and 88% for the CDTect assay, resp. In a population from a birth cohort study, consisting of 21-yr-old males and females with less excessive alc. consumption, the correlation between AXIS %CDT and CDTect CDT was weaker but still statistically significant ($r = 0.46$, $n = 212$, $P < 0.001$). In this population, with specificities >83% in detecting

alc. consumption levels of .gtoreq.6 drinks per wk, the sensitivities were low with both CDT assays (<43% for .gtoreq.6 drinks per wk, and <44% for .gtoreq.16 drinks per wk). These results suggest that (a) both assays are equally effective in detecting chronic drinking over 60 g/day in older alc. males, and (b) both assays are similarly ineffective in detecting less excessive regular drinking in young males and females.

L161 ANSWER 16 OF 32 BIOSIS COPYRIGHT 2000 BIOSIS

1997:126837 Document No.: PREV199799418650. Increased serum concentration of carbohydrate-deficient transferrin in patients with combined pancreas and kidney transplantation. Arndt, Torsten (1); Hackler, Rolf; Mueller, Thomas; Kleine, Tilman O.; Gressner, Axel M.. (1) Institut fuer Laboruntersuchungen Ingelheim GmbH, Hamburger Str. 1, D-55218 Ingelheim Germany. Clinical Chemistry, (1997) Vol. 43, No. 2, pp. 344-351. ISSN: 0009-9147. Language: English.

AB Serum concentration of carbohydrate-deficient transferrin (cCDT) is used for laboratory diagnosis and follow-up of chronic alcohol abuse. In analyzing by CDTect-RIA (Pharmacia) sera from

outpatients with combined pancreas and kidney transplantation and no excessive alcohol consumption, we found above-normal values for cCDT and CDT/transferrin ratios (CDT/Tf) in more than half of the samples. Isoelectric focusing of these samples showed

distinct

bands of carbohydrate-deficient isotransferrins, supporting the abnormal findings from the CDTect assay. In contrast, diabetics and outpatients who had received only kidney transplants showed normal values for cCDT, CDT/Tf, and isotransferrin patterns. Increased serum Tf, sialidase-producing microorganisms, and immunosuppressive medication were eliminated as causes

of these abnormal cCDT and CDT/Tf results. Successful pancreas transplantation leads to hyperinsulinemia and normoglycemia, in contrast to hypoinsulinemia and hyperglycemia in the patients who receive kidney transplants alone. These factors may have pathogenic importance for CDT increase, yielding results falsely interpreted as positive with respect

to

alcohol abuse in patients with combined pancreas and kidney transplantation.

L161 ANSWER 17 OF 32 MEDLINE

97259387 Document Number: 97259387. Biochemical markers of alcohol use and abuse: experiences from the Pilot Study of the WHO/ISBRA Collaborative Project on state and trait markers of alcohol. International Society for Biomedical Research on Alcoholism. Helander A; Tabakoff B. (Karolinska Institute, Department of Clinical Neuroscience, St Gorans Hospital, Stockholm, Sweden.) ALCOHOL AND ALCOHOLISM, (1997 Mar-Apr) 32 (2) 133-44. Journal code: AAL. ISSN: 0735-0414. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The development of reliable diagnostic tools for assessing alcoholism and harmful alcohol consumption is an utmost necessity for the success of efforts to prevent and treat alcohol-induced damage to both individuals and to society. A multinational

study is underway to aid in the development of biological screening tools
Prepared by M. Hale 308-4258 Page 46

(state markers) which can, with good sensitivity and specificity, identify problem drinkers. To attain this goal information needs to be available on an individual's drinking history and habits and related factors. A detailed instrument has been developed to obtain this information. The second goal of the study was to begin to develop diagnostic 'trait markers' which provide biological information on genetically determined predisposing and protective factors in the development of alcoholism. The developed questionnaire also provides background information on subject characteristics necessary for the development of trait markers. Centres will assay the obtained biological samples for 'traditional' and newly identified state markers of excessive alcohol consumption. These will include methanol measurements, gamma-glutamyltransferase, aspartate aminotransferase, carbohydrate-deficient transferrin, serotonin metabolite ratios, and erythrocyte aldehyde dehydrogenase. DNA obtained from the lymphocytes of subjects will be assayed for polymorphisms of alcohol- and aldehyde-metabolizing enzymes and dopamine receptor polymorphisms which can provide insights into protective and predisposing factors in alcoholism. The platelet enzymes, monoamine oxidase and adenylyl cyclase, will be assayed to assess the relationships between these putative trait markers and the genetic and environmental factors contributing to the aetiology of alcoholism. The current report is meant to introduce the study design and present a portion of the preliminary data gathered in the process of establishing this research programme.

L161 ANSWER 18 OF 32 CAPLUS COPYRIGHT 2000 ACS
1997:172133 Document No. 127:77040 Clinical value of two methods for the determination of carbohydrate-deficient transferrin. Lyngbye, Jorgen; Eide, Arne; Walter, Henriette; Semler, Brigitte; Winkler, Franz; Lesch, Otto Michael (Department Clinical Chemistry, Molde Hospital, Molde, N-6400, Norway). Clin. Lab. (Heidelberg), 43(1+2), 53-55 (English) 1997. CODEN: CLLAfp. Publisher: Clin Lab Publications.

AB The routine assays CDTect and Axis%CDT RIA for the detn of carbohydrate-deficient transferrin (CDT) and their use in monitoring alc. abuse were compared. The subjects investigated were divided into groups of comprised chronic alcoholics, social drinkers, total abstainers, and pregnant women. A correlation between methods and a specificity for alc. intake in all groups were demonstrated. CDT was elevated in 10.5% pregnant women without alc. intake by the CDTect method only. Both methods are well suited for monitoring alc. abuse.

L161 ANSWER 19 OF 32 MEDLINE DUPLICATE 10
96330460 Document Number: 96330460. Sensitivity and specificity of carbohydrate-deficient transferrin as a marker of alcohol abuse are significantly influenced by alterations in serum transferrin: comparison of two methods. Sorvajarvi K; Blake J E; Israel Y; Niemela O. (EP Central Hospital Laboratory, Seinajoki, Finland.) ALCOHOLISM, CLINICAL AND EXPERIMENTAL RESEARCH, Prepared by M. Hale 308-4258 Page 47

(1996 May) 20 (3) 449-54. Journal code: 35X. ISSN: 0145-6008. Pub. country: United States. Language: English.

AB Despite a number of investigations suggesting the value of **carbohydrate-deficient transferrin** (CDT) as a marker of alcohol abuse, a variety of issues on the applicability of CDT measurements in clinical settings have remained unexplored. Earlier studies in this field have focused on the relationship of CDT and the amount of **alcohol consumption** or presence of liver disease, whereas the influence of alterations in serum **transferrin** concentrations on CDT has received less attention. In this study, we compared two different **methods** for measuring CDT (CDTect and %CDT) and total **transferrin** concentrations in a sample of 83 alcohol abusers (20 patients with alcoholic liver disease and 63 heavy drinkers who were devoid of liver disease, despite excessive **alcohol consumption**) and 89 controls, who were social drinkers or abstainers. The control population included 53 hospitalized patients with expected abnormalities in serum **transferrin** concentrations caused by conditions such as negative iron balance, pregnancy, or nonalcoholic liver disease. Both **methods** gave significantly higher values in alcohol abusers than in controls ($p < 0.01$), but the overall sensitivity for detecting alcohol abuse was clearly higher for CDTect (59%) than for %CDT (34%). The correlation between the results obtained by the two **methods** ($r = 0.629$) significantly improved, when the CDTect values were replaced by the ratio of CDTect/total **transferrin** ($r = 0.770$) ($p < 0.05$). There was a positive correlation between the CDTect and serum **transferrin** ($r = 0.201$, $p < 0.01$), which was significant both in the alcoholics ($r = 0.240$, $p < 0.05$), and especially in the controls ($r = 0.727$, $p < 0.001$).

A significant inverse correlation emerged between %CDT and total **transferrin** ($r = -0.302$, $p < 0.01$). The sensitivities of CDTect and %CDT for correctly classifying alcohol abusers in the subgroup of alcoholic liver disease patients were 90% and 70% and in the subgroup of heavy drinkers without liver disease (49% and 22%), respectively. Specificities for CDTect and %CDT in this sample were 81% and 100%, respectively. However, in the subgroup of hospitalized control patients with abnormal serum **transferrin**, the specificity of CDTect was only 48%. According to present data, CDTect seems to be more sensitive than %CDT for detecting alcohol abuse. However, any alteration in serum total **transferrin** concentration markedly decreases the assay specificity. This should be considered when interpreting the assay results in patients with elevated serum **transferrin**, such as iron deficiency, pregnancy, or liver diseases.

L161 ANSWER 20 OF 32 BIOSIS COPYRIGHT 2000 BIOSIS
1996:263043 Document No.: PREV199698819172. Effect of cationic buffer additives on the capillary electrophoretic separation of serum **transferrin** from different species. Oda, Robert P.; Landers, James P. (1). (1) Clin. CE Fac., Dep. Lab. Med. Pathol., Hilton 920, Mayo

Clin., Rochester, MN 55905 USA. Electrophoresis, (1996) Vol. 17, No. 2, pp. 431-437. ISSN: 0173-0835. Language: English.

AB The presence of specific **transferrin** (Tf) glycoforms in human serum has been shown to correlate with certain clinical syndromes. Hence, the ability to separate and quantitatively measure the various forms of **transferrin** has been demonstrated. Prepared by M. Hale 308-4258 Page 48

human **transferrin** has become increasingly important. As a means of evaluating the potential for developing a rapid capillary electrophoresis-based assay for the analysis of **carbohydrate-deficient transferrins** (CDTs), the capillary zone electrophoretic (CZE) analysis of Tfs from several species was evaluated using uncoated capillaries and a separation augmented with cationic additives. With bovine Tf, five peaks (representing different sialylated forms) were partially resolved in borate and baseline-resolved when 1,4-diaminobutane was added to the buffer. These same conditions were found to be inadequate for the resolution of the sialoforms from other species. Some success was achieved using alpha,omega-bis-quaternary ammonium alkanes instead of the 1,4-diaminobutane and optimizing the pH for each of the species' Tfs.

Human

Tf was found to be resolved in an uncoated capillary equilibrated with a borate buffer containing millimolar concentrations of decamethonium bromide as a buffer additive. Under these conditions, resolution of the various sialoforms from the iron-saturated Tf was possible and the glycoforms were found to migrate differently than their iron-depleted counterparts. Despite the resolution achievable under these conditions, the lengthy analysis time is incompatible with the requirements for a clinical CZE-based assay.

L161 ANSWER 21 OF 32 MEDLINE

DUPLICATE 11

96248150 Document Number: 96248150. **Carbohydrate-deficient transferrin** for identification of drug overdose patients at risk of an alcohol withdrawal syndrome. Koppel C; Muller C; Wrobel N. (Poison Information Center, Department of Internal Medicine, Berlin, Germany.) JOURNAL OF TOXICOLOGY. CLINICAL TOXICOLOGY, (1996) 34 (3) 297-300. Journal code: KAN. ISSN: 0731-3810. Pub. country: United States.

Language:

English.

AB BACKGROUND: Chronic alcohol abuse is frequent in patients admitted to the intensive care unit with acute drug overdose. During detoxification, an alcohol withdrawal syndrome may develop in patients with a history of chronic alcohol abuse. Withdrawal or delirium is associated with serious risks, necessitating early identification of patients at risk. Since the information obtained from the patients or their relatives on **alcohol consumption** is often unreliable, biochemical markers may be helpful. **Carbohydrate deficient transferrin** is considered a highly specific marker (reported maximum specificity 97%, sensitivity 40-85%) for identifying alcohol abuse. METHODS: In 20 patients with acute drug overdose and suspected alcohol abuse, **carbohydrate deficient transferrin** was determined by an immunoturbidimetric assay on admission to the intensive care unit. Eight of the patients had **carbohydrate deficient transferrin** levels above the "positive" threshold and nine in a suspicious range. A "false" negative **carbohydrate deficient transferrin** was found in three patients who were thought to have changed their drinking habits prior to hospitalization. A "positive" **carbohydrate deficient transferrin** test is assumed to be associated with ingestion of more than 60-80 g ethanol/d for a period of more than seven days.

RESULTS:

Prepared by M. Hale 308-4258

Page 49

In all patients, clonidine (30-210 micrograms/h i.v.) was started. None developed delirium. Since alcohol addiction is frequently denied, **determination of carbohydrate deficient transferrin** may be useful for its early diagnosis but the sensitivity of this parameter requires further evaluation.

L161 ANSWER 22 OF 32 CAPLUS COPYRIGHT 2000 ACS

1995:753704 Document No. 123:309893 **Assay for glycosylation deficiency disorders.** Bean, Pamela; Terryberry, Jeff W. (Specialty Laboratories Inc., USA). U.S. US 5432059 A 19950711, 11 pp. (English). CODEN: USXXAM. APPLICATION: US 1994-222422 19940401.

AB A method is provided for detecting **carbohydrate-deficient** glycoproteins in samples taken from subjects with metabolic disorders, such as alc. abuse and subjects who display a syndrome of carrying abnormal levels of **carbohydrate-deficient** glycoproteins. The method involves steps of reglycosylating with a fluorescent-conjugate deglycosylated glycoproteins in a sample of **body fluid** from a subject. A further step involves fluorometric detection of fluoresceinylated carbohydrates incorporated into truncated serum glycoproteins.

L161 ANSWER 23 OF 32 MEDLINE

DUPLICATE 12

95267122 Document Number: 95267122. Diagnostic tests for **alcohol consumption.** Conigrave K M; Saunders J B; Whitfield J B. (Centre for Drug and Alcohol Studies, Royal Prince Alfred Hospital, Camperdown, Sydney, NSW, Australia.) ALCOHOL AND ALCOHOLISM, (1995 Jan) 30 (1)

13-26.

Ref: 105. Journal code: AAL. ISSN: 0735-0414. Pub. country: ENGLAND: United Kingdom. Language: English.

AB A variety of laboratory tests are available to assist in the diagnosis of hazardous **alcohol consumption** and related disorders. Standard tests, such as serum gamma glutamyltransferase activity and erythrocyte mean cell volume, have limited sensitivity, particularly in detecting non-dependent hazardous consumption. Most also have poor specificity in that results are affected by common diseases and medications. Over the past 10 years a number of new laboratory tests have emerged. One of these, **carbohydrate deficient transferrin**, has high sensitivity in detecting persons with alcohol dependence, and shows promise for identification of non-dependent hazardous drinking; it is also highly specific. Others such as measurement

of bound acetaldehyde, serum beta-hexosaminidase and the ratio of urinary serotonin metabolites offer promise in detecting recent heavy drinking. However, many issues remain unresolved. The newer markers have often been judged by contrasting their values in patients who are clearly alcohol dependent and abstainers or very light drinkers. It is now apparent that some are relatively insensitive markers of hazardous consumption. Future research needs to examine the performance of these markers among subjects with a range of alcohol intakes to fully **determine** their value in assessing drinking history. In addition, **assays** which are capable of some degree of automation need to be developed for analysing large numbers of samples.

L161 ANSWER 24 OF 32 MEDLINE

DUPLICATE 13

94177716 Document Number: 94177716. Two **methods** for measuring **carbohydrate-deficient transferrin** in

Prepared by M. Hale 308-4258

Page 50

inpatient alcoholics and healthy controls compared. Anton R; Bean P. (Medical University of South Carolina, Charleston 29425-0742.) CLINICAL CHEMISTRY, (1994 Mar) 40 (3) 364-8. Journal code: DBZ. ISSN: 0009-9147. Pub. country: United States. Language: English.

AB **Carbohydrate-deficient transferrins (CDTs),** naturally occurring glycosylated **transferrin** proteins, are reported to be increased in the serum of individuals who consume large quantities of alcohol (ethanol). We compared two **methods** for the separation and quantification of CDT, using the same alcohol-dependent patients and age-, gender-, and race-matched controls as sources of samples for both **assays**. There was good correlation ($r = 0.89$) between the microcolumn anion-exchange chromatography/RIA (MAEC/RIA) procedure and the isoelectric focusing, immunoblotting, and laser densitometry (IEF/IB/LD) procedure. Receiver operating characteristic analysis suggested that the IEF/IB/LD procedure would perform slightly better than MAEC/RIA for the overall population. However, both **assays** were much more sensitive for the detection of heavy alcohol consumption in men, compared with women. **Alcohol consumption** in the week prior to CDT measurement correlated only weakly with the concentrations measured with either **assay**.

L161 ANSWER 25 OF 32 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
94145845 EMBASE Document No.: 1994145845. **Carbohydrate-deficient transferrin** during 3 weeks' heavy alcohol consumption. Salmela K.S.; Laitinen K.; Nystrom M.; Salaspuro M.. Research Unit of Alcohol Diseases, University of Helsinki, Tukholmankatu 8 F, SF-00290 Helsinki, Finland. **Alcoholism: Clinical and Experimental Research** 18/2 (228-230) 1994. ISSN: 0145-6008. CODEN: ACRSDM. Pub. Country: United States. Language: English. Summary Language: English.

AB To study the effect of controlled heavy drinking of 60 g ethanol/day for 3 weeks on **carbohydrate-deficient transferrin** (CDT), a commercial double antibody kit (CDTect(TM)) was used. By the end of the third drinking week, a statistically significant increase in the mean CDT level was observed. When compared to AST and γ -glutamyltransferase, CDT was a more informative marker. However, only in 2 of the 10 volunteers did CDT exceed the upper normal level (20 units/liter) recommended by the manufacturer. This indicates that the sensitivity of CDT to detect heavy drinking is lower than that previously reported. The higher accuracy has in general been obtained in studies comparing healthy controls with a low alcohol consumption to alcoholics with an alcohol consumption higher than that used in the present experiment. Our results suggest that it remains to be established whether CDT, although better than AST and γ -glutamyltransferase, will provide a clinically useful tool in identifying heavy drinkers in populations covering a wide range of alcohol consumption.

L161 ANSWER 26 OF 32 MEDLINE
94310384 Document Number: 94310384. Serum alpha-fetoprotein and alcohol consumption. Christiansen M; Andersen J R; Torning J; Overgard O; Jensen S P; Magid E; Norgaard-Pedersen B. Prepared by M. Hale 308-4258 DUPLICATE 14 Page 51

(Department of Clinical Biochemistry, Statens Serum Institut, Copenhagen.

) SCANDINAVIAN JOURNAL OF CLINICAL AND LABORATORY INVESTIGATION, (1994 May)
54 (3) 215-20. Journal code: UCP. ISSN: 0036-5513. Pub. country:

ENGLAND:

United Kingdom. Language: English.
AB Fifty-nine persons, 23 chronic alcoholics and 36 normal healthy persons with a well described **alcohol consumption**, had the serum concentration of alpha-fetoprotein **determined** by a sensitive monoclonal immunofluorescent **assay**. A significant elevation in S-AFP was found in alcoholics, median 4.1 kIU/l as compared to 3.0 kIU/l in near-abstainers (< 12 g ethanol per day) ($p < 0.02$). This difference was not explained by differences in age. S-AFP correlated positively with age ($p = 0.01$). In non-alcoholics a borderline significant correlation with S-AFP was found with average daily **alcohol consumption** (self-reported) ($p = 0.09$) and a significant correlation with the serum concentration of **carbohydrate-deficient transferrin** (S-CDT) ($p = 0.004$). In 11 alcoholics 2 months of abstention from alcohol was accompanied by a median reduction of 21% in S-AFP ($p < 10(-5)$). In alcoholics, but not in social drinkers, S-AFP correlated with S-ASAT ($p = 0.004$). The increase of S-AFP with **alcohol consumption** may reflect reversible alcohol-induced liver affection.

L161 ANSWER 27 OF 32 MEDLINE

DUPLICATE 15

94084919 Document Number: 94084919. Semi-automatic **method** for determination of different isoforms of **carbohydrate-deficient transferrin**. Lof K; Koivula T; Seppa K; Fukunaga T; Sillanaukee P. (Biomedical Research Center, Alko Ltd, Department of Clinical Chemistry.) CLINICA CHIMICA ACTA, (1993 Aug 31) 217 (2) 175-86. Journal code: DCC. ISSN: 0009-8981. Pub. country: Netherlands. Language: English.

AB **Carbohydrate deficient transferrin** (CDT) has been reported to be one of the best biochemical markers of alcohol abuse. However, a need still exists for a simple and practical **method** for widespread laboratory use. A semi-automatic (SA) isoelectric focusing (IEF) **assay** for CDT (SA-IEF-CDT) by a Phast System is introduced here. Different isoforms of **transferrin** were separated by IEF on polyacrylamide gels (pI 4.0-6.5) and located by immunofixation with an **anti-transferrin** serum. The precipitation bands were stained with Coomassie Brilliant Blue and quantitated densitometrically. The present **method** gave a picture of the relative amounts of 10 different **transferrin** isoforms. The percentage of CDT with $pI > or = 5.7$ (representing di-, mono- and **asialotransferrin**) was calculated. For comparisons **transferrin** bands with $pI > or = 5.6$ (tri-, di-, mono-, and **asialotransferrin**), $pI > or = 5.8$ (mono- and **asialotransferrin**) and $pI > or = 5.9$ (**asialotransferrin**) as well as GGT, ASAT and ALAT were calculated. The **method** showed good linearity and it identified different isoforms in concentrations of < 10 mg/l of **transferrin**. The correlation of the present **method** with a commercially available **method** employing anion exchange followed by double antibody RIA (AE-RIA-CDT) was good ($n = 38$, $r = 0.924$). In 19/20 (95%) of healthy controls, the CDT value was below 4.4% (mean + 2 S.D.) of total

Prepared by M. Hale 308-4258

Page 52

transferrin, while higher values were observed in all 20 (100%) alcoholics. In conclusion, the developed semi-automatic method is a practical and reliable alternative for determination of different transferrin isoforms.

L161 ANSWER 28 OF 32 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
94092699 EMBASE Document No.: 1994092699. Serum level of carbohydrate-deficient transferrin as a marker of alcoholic liver disease. Yamauchi M.; Hirakawa J.; Maezawa Y.; Nishikawa F.; Mizuhara Y.; Ohata M.; Nakajima H.; Toda G.. First Dept of Internal Medicine, Jikei University School of Medicine, 3-25-8 Nishi-Shinbashi, Minato-ku, Tokyo 105, Japan. Alcohol and Alcoholism 28/SUPPL. 1 B (3-8) 1993.
ISSN: 0735-0414. CODEN: ALALDD. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Serum levels of carbohydrate-deficient transferrin (CDT) were assayed in 87 patients with alcoholic liver disease, 25 alcoholics without liver disease, 25 cases with viral liver disease and 37 healthy subjects, by two different methods (Pharmacia CDT RIA kit and Axis % CDT kit). The serum level of Pharmacia-CDT was significantly higher in the patients with alcoholic liver disease (38.9 .+- .2.8 U/l) compared to the normal subjects (18.9 .+- .0.2 U/l), alcoholics without liver disease (21.7 .+- .1.5 U/l) and non-alcoholic liver disease (viral liver disease) (23.4 .+- .1.6 U/l) (P <

0.001). The serum level of Axis-CDT was also significantly higher in the patients with alcoholic liver disease (4.22 .+- .0.48%) compared to the normal subjects (0.84 .+- .0.14%), alcoholics without liver disease (1.14 .+- .0.23%) and non-alcoholic liver disease (1.84 .+- .0.29%) (P <

0.001). A significant correlation was found between serum levels of CDT determined by the two kits ($r = 0.718$, $P < 0.001$). The serum level of Axis-CDT was significantly higher in patients with alcoholic hepatitis compared to the normal subjects ($P < 0.005$), while the serum level of Pharmacia-CDT was not increased in the patients with alcoholic hepatitis. These results indicate that determination of serum CDT levels is a useful marker of alcoholic liver disease, not a marker for alcohol consumption. Axis-CDT is more useful than Pharmacia-CDT for assaying the serum level of CDT in patients with alcoholic liver disease.

L161 ANSWER 29 OF 32 MEDLINE DUPLICATE 16
93371566 Document Number: 93371566. A modified method for the assay of carbohydrate-deficient transferrin (CDT) in serum. Stibler H; Borg S; Joustra M. (Department of Neurology, Karolinska Hospital, Stockholm, Sweden.) ALCOHOL AND ALCOHOLISM. SUPPLEMENT, (1991) 1 451-4. Journal code: AAP. ISSN: 1358-6173. Pub. country: ENGLAND: United Kingdom. Language: English.

AB CDT has been shown to be a good marker of regular high alcohol intake. It has been measured principally by isoelectric focusing or pH-based anion exchange chromatography. The present assay was developed to improve the technical stability of the latter method. It is based on anion exchange of serum using ionic strength instead of pH followed by a transferrin in RIA of isotransferrins with $pI > 5.7$. Two hundred and fifty-one individuals were examined. With the exception of a new inborn error of glycoprotein metabolism, the

sensitivity for alcohol abuse was 94% and the specificity was 98%. The values correlated with the total amount of alcohol recently consumed and normalized with a mean t1/2 of 15 days.

L161 ANSWER 30 OF 32 CAPLUS COPYRIGHT 2000 ACS

1988:452324 Document No. 109:52324 **Transferrin phenotype and level of carbohydrate-deficient transferrin in healthy individuals.** Stibler, Helena; Borg, Stefan; Beckman, Gunhild (Dep. Neurol., Karolinska Hosp., Stockholm, 104 01, Swed.). *Alcohol.: Clin. Exp. Res.*, 12(3); 450-3 (English) 1988. CODEN: ACRSDM. ISSN: 0145-6008.

AB Elevated concns. of **carbohydrate-deficient** components of **transferrin** (CDT) in serum may be used as a sensitive and specific marker of regular, high alc. **consumption**. When **detd.** by a new, simplified **assay**, CDT values are nearly normally distributed in low- or nonalc.-consuming control populations. The importance of **transferrin** phenotype for this normal variation was analyzed in healthy, European men and women with no or negligible alc. intake. No significant relation was found between phenotype and CDT value in this population. The 3 rare B-variants found had low CDT levels, and examn. of 1 subject, outside the study, with a rare D-variant indicated that D-variants may result in false-pos. CDT values. Moreover, women tended to have somewhat higher values than men, in whom CDT levels were weakly correlated with age. Other as yet undefined biol. factors are clearly responsible for the major part of the nominal variation of CDT values in nonalcoholic individuals.

L161 ANSWER 31 OF 32 MEDLINE

DUPLICATE 17

89117803 Document Number: 89117803. **Carbohydrate-deficient transferrin** (CDT) in serum in women with early alcohol addiction. Stibler H; Dahlgren L; Borg S. (Department of Neurology, Karolinska Hospital, Stockholm, Sweden.) *ALCOHOL*, (1988 Sep-Oct) 5 (5) 393-8. Journal code: AG9. ISSN: 0741-8329. Pub. country: United States.

Language:

English.

AB **Carbohydrate-deficient transferrin** (CDT) in serum was determined by micro anion exchange chromatography and a **transferrin radioimmune assay** in 58 consecutive women treated for early alcohol dependence compared, with 62 healthy females with an **alcohol consumption** of 0-15 g of ethanol/day. The upper normal CDT level was 74 mg/l. CDT was elevated above this value in 83% of the alcoholic women with an intake of 60 g of ethanol/day or more for at least 7 days within the preceding two weeks. CDT values were significantly positively correlated with daily **alcohol consumption** but not with GT, ASAT, ALAT or MCV. During abstinence CDT level declined exponentially with a half-life of 14 +/- 3 days. The results indicated that CDT may be as sensitive and specific a marker in women with early alcohol addiction as in previously studied male alcoholics. The amount of alcohol consumed appeared to be more important than sex or liver function. **Determination** of CDT may thus offer a means for early objective diagnosis and adequate treatment also of women in early stages of **alcoholism**.

L161 ANSWER 32 OF 32 MEDLINE

DUPLICATE 18

87097874 Document Number: 87097874. **Micro anion exchange chromatography of carbohydrate-deficient transferrin in serum in** Prepared by M. Hale 308-4258

Page 54

relation to alcohol consumption (Swedish Patent 8400587-5). Stibler H; Borg S; Joustra M. ALCOHOLISM, CLINICAL AND EXPERIMENTAL RESEARCH, (1986 Oct) 10 (5) 535-44. Journal code: 35X.

ISSN:

0145-6008. Pub. country: United States. Language: English.

AB A new simplified and rapid **method** for detection and quantitation of "carbohydrate-deficient transferrin" in serum is described. The **method** is based on isocratic anion exchange chromatography of **isotransferrins** in disposable microcolumns followed by a double antibody **transferrin radioimmune assay**. This technique, which separates all **transferrin** components isoelectric above pH 5.65, showed a very good reproducibility and accuracy with a coefficient of variation between 5 and 9%. 77 alcoholic patients could be clearly separated from 80 healthy "normal consumers" and 33 total abstainers with a specificity of 100% and a sensitivity of 91%. The values were significantly correlated to the amount of alcohol consumed during the latest month, and declined in abstaining alcoholics with a mean biological half-life of 17 days. Elevated levels occasionally appeared in healthy individuals after daily consumption of 60 g of ethanol during a 10-day period. In a sample of 187 patients with nonalcohol-related conditions only 2% false-positive values were found. This **method** is suggested as a potential tool for detecting and monitoring alcohol abuse.

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	304.21	308.56
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-10.57	-10.57

STN INTERNATIONAL LOGOFF AT 10:49:32 ON 13 SEP 2000